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ABSTRACTS OF WORLD MEDICINE

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ABSTRACTS OF WORLD MEDICINE

This journal is planned to provide the reader with a selection of abstracts of the more important articles appearing in medical periodicals published in different parts of the world. Comment by the abstracter, when thought necessary, is inserted between square brackets, usually at the end of an abstract. In some instances only the titles of articles are provided.

The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals* and in *World Medical Periodicals*. The titles of articles from foreign journals are translated into English.

This journal is essentially a guide to work in progress in the world's medical centres. No abstract can be regarded as a substitute for the article abstracted. For complete information the original article must be consulted. Our aim is to give the reader sufficient details in an abstract to enable him to judge whether the original is, for him, worth reading in full.

The abstracts are grouped in broad classifications and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together under the same heading. The specialist will, it is hoped, learn from this journal of work done in other fields as well as in his own. The general practitioner will be able to keep abreast of modern knowledge in the various specialties. The representation in one journal of the several aspects of Medicine will, it is believed, give an integrated picture of the whole, necessary in this age of specialization.

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EXPERIMENTAL PATHOLOGY

904 (*a*). **The Effect of Cortisone and Streptomycin on Experimentally Induced Pulmonary Tuberculosis in Rabbits**

T. E. MORGAN, S. H. WANZER, and D. T. SMITH. *Journal of Bacteriology* [*J. Bact.*] **67**, 257–263, March, 1954. 2 figs., 20 refs.

904 (*b*). **The Effect of Corticotropin (ACTH) and Streptomycin on Experimentally Induced Pulmonary Tuberculosis in Rabbits**

S. H. WANZER, T. E. MORGAN, and D. T. SMITH. *Journal of Bacteriology* [*J. Bact.*] **67**, 264–270, March, 1954. 2 figs., 13 refs.

These two papers are concerned with experiments performed at Duke University School of Medicine, Durham, N. Carolina, which were designed to compare the effects of cortisone and corticotrophin (ACTH) on the progress of pulmonary tuberculosis in rabbits under treatment with streptomycin. All the animals employed in the experiments were of approximately the same weight, but of mixed sexes. [Presumably they were of the same strain; the authors describe them simply as white rabbits.] Some of the animals had previously been sensitized and partially immunized by the subcutaneous injection of a homogenate of living, avirulent tubercle bacilli. Infection was induced by the injection of a standard dose of *Mycobacterium tuberculosis* var. *bovis*, Ravenel strain, into the trachea, the rabbit being held so that the inoculum drained into the upper lobe of the right lung. The 149 rabbits so infected were divided into 10 groups, 4 of which were unsensitized and 6 sensitized, and were treated as follows: (A) *Unsensitized animals*: (I) controls (untreated); (II) streptomycin only; (III) cortisone or ACTH only (low dosage); (IV) streptomycin plus cortisone or ACTH (low dosage). (B) *Sensitized animals*: (I) controls (untreated); (II) streptomycin only; (III) cortisone or ACTH only (low dosage); (IV) streptomycin plus cortisone or ACTH (low dosage); (V) cortisone or ACTH only (high dosage); (VI) streptomycin plus cortisone or ACTH (high dosage). The rabbits died or were killed at different intervals and the extent of the disease determined.

In general the disease was much more extensive in the unsensitized than in the sensitized animals, while those receiving streptomycin were less severely affected than the rest. When cortisone was given alone in low dosage the lesions present in both sensitized and non-sensitized groups were more severe and more progressive than those seen in the controls, and when high doses were given the condition was fulminating and invariably fatal. Cortisone in low dosage plus streptomycin gave a picture similar to that seen with streptomycin alone, whereas the condition of the animals receiving cortisone in high dosage plus streptomycin was more like that of the untreated controls. In contrast to cortisone, ACTH in low dosage did not exert any damaging effect on the course of untreated tuberculosis, nor did it interfere with the beneficial effect of streptomycin. Even in high dosage it did not interfere with the action of streptomycin, and when given alone the disease was only a little more severe than that seen in the controls. The low dosage of cortisone used (2 mg. daily) was approximately equivalent to the usual dosage for man (60 to 200 mg.), whereas the low dosage of ACTH (10 units daily) was well above the equivalent human dosage. The higher dosages of cortisone and ACTH were 20 mg. and 20 units daily respectively. Cortisone thus exerted a deleterious effect both at and above the normal dosage level, whereas no harmful effect was seen with ACTH until the dosage was 20 times greater than normal.

H. J. Bensted

905. **The Permeability of Lung Parenchyma to Particulate Matter**

P. GROSS and M. WESTRICK. *American Journal of Pathology* [*Amer. J. Path.*] **30**, 195–213, March–April, 1954. 8 figs., 35 refs.

The authors, working at the Industrial Hygiene Foundation, Pittsburgh, have carried out experiments to determine if dust particles *per se* can penetrate the pulmonary parenchyma or if they are merely carried there by wandering macrophages, as most authors have held hitherto. In one series of experiments excised lungs of freshly killed rats were mechanically "respired" with air heavily charged with carbon dust. In another series indian ink was injected intratracheally into rats and the animals killed 4 hours to 4 days later. Examination of sections of the lungs showed the interstitial tissues in the first series of experiments to be oedematous and to have innumerable minute carbon particles scattered diffusely throughout the fluid, this being most marked around vessels and bronchi. In the second series foci of carbon particles were seen mainly about the larger vessels and bronchi.

Although it could not be demonstrated, it is believed that particles penetrate the respiratory membrane through pre-existing minute erosions and, having gained admis-

sion, are caused to move by the normal excursionary activity of the lung tissue. If pneumonia is induced the flow of tissue fluid is initially towards the alveoli and the migration of particles is thus inhibited. In this study pains were taken to exclude various artefacts which might arise during the experiments. In reply to supporters of the macrophage theory, who suggest that anthracotic pigment in the lungs is due to disintegration of macrophages, the authors point out that the decisions regarding the intracellular position of pigment made by these workers must be based largely upon conjecture and are not susceptible of demonstration, since cell outlines are rarely distinguishable and nuclei generally cannot be seen, so that identification of the cells is impossible.

E. G. Rees

906. **The Experimental Production of Bronchiectasis in Rats**

KWOK-KEW CHENG. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **67**, 89–98, Jan., 1954. 11 figs., 24 refs.

The effects of bronchial ligation in rats, leading to the development of bronchiectasis, were observed for periods up to 2 months. The findings suggest that the most important aetiological factors in bronchiectasis are bronchitis and stagnation of the accompanying secretions. When stagnation is marked, bronchiectasis always occurs, whereas the accompanying pneumonitis is secondary and of no importance. Negative intrathoracic pressure resulting from pulmonary collapse did not appear to be important, as oleothorax did not prevent the development of bronchiectasis after ligation of the bronchus. Release of the bronchial ligature after some days resulted in "dry" bronchiectasis. It is considered that these findings may have some bearing on the development of some types of human bronchiectasis.

G. J. Cunningham

907. **Bacterial Endocarditis: an Experimental Study of Healing**

M. G. MCGEOWN. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **67**, 179–186, Jan., 1954. 9 figs., 8 refs.

In experiments performed at Queen's University, Belfast, bacterial endocarditis was induced in 18 rabbits by producing a serum valvulitis and subsequently injecting *Streptococcus viridans* intravenously, 12 of the animals being given 300,000 units of procaine penicillin daily, starting as soon as signs of ill health became apparent, and the remainder being left untreated as controls. The animals were killed after varying intervals, and a complete post-mortem examination made as soon as possible. The stages of healing in treated and untreated animals were essentially similar, and closely resembled those seen in man. Small vegetations tended to become replaced by granulation tissue and to heal from the base, whereas larger vegetations were endothelized and healed in part from the base. From the smaller lesions the bacteria were completely removed, but they persisted in the centre of the larger lesions, which became calcified later. The author points out that although penicillin has greatly improved the prognosis of bacterial endocarditis, it does not appear to change the nature of the healing process, and he suggests that if it were possible to modify the latter so that calcification was retarded or inhibited, a better functional result might be obtained.

G. J. Cunningham

908. **The Problem of the Haemostatic Effect of Painful Stimuli and of Adrenaline.** (К вопросу о гемостатическом эффекте болевого раздражения и адреналина)

N. S. DZHAVADYAN. *Архив Патологии* [*Arkh. Patol.*] **16**, 22–33, Jan.–March, 1954. 2 figs., 9 refs.

The author has previously shown in dogs that the application of painful stimuli or the injection of adrenaline results in thrombocytosis, hyperthrombinaemia, and acceleration of the clotting time. He now reports the results of further investigations into the mechanism of this phenomenon, and particularly into the role played in it by the liver, spleen, and lungs. The experiments were again performed on dogs, some of which were splenectomized, blood being taken from the portal and hepatic veins, from the femoral artery and vein, and from the right and left sides of the heart before and after the application of an electric current or the injection of adrenaline.

The results suggest that the liver, through the production of thrombin and fibrinogen, is active in the regulation of blood coagulation, a painful stimulus or injection of adrenaline causing an increase in these functions of the liver. There is some indication that the lungs serve as the chief storage depot for blood platelets, which are possibly formed there, the rapid increase in the number of blood platelets in the circulating blood perhaps being accounted for by their being washed out of the lungs.

L. Crome

909. **Suppression by Cortisone of Granuloma Formation and Antibody in Guinea Pigs Receiving Egg Albumin with Freund Adjuvants**

E. E. FISCHEL, E. A. KABAT, H. C. STOERK, M. SKOLNICK, and A. E. BEZER. *Journal of Allergy* [*J. Allergy*] **25**, 195–200, May, 1954. 1 fig., 24 refs.

In a study made at Columbia University College of Physicians and Surgeons, New York, of the effect of cortisone on granuloma formation and antibody level, guinea-pigs were sensitized by injection of egg albumen mixed with paraffin oil containing heat-killed tubercle bacilli (Freund adjuvant). The animals were bled 2 to 4 weeks after the last sensitizing injection and the antibody nitrogen per ml. of serum determined. One group of animals received 5 mg. and another group 25 mg. of cortisone by intramuscular injection daily for 4½ weeks from 3 days before sensitization onwards.

The antibody level and the degree of granuloma formation at the injection site were not significantly different in a control group and the group receiving 5 mg. of cortisone. The group receiving 25 mg. of cortisone, however, produced much less antibody than the others, and showed little granuloma formation. The mortality in the group receiving 25 mg. of cortisone was high, 11 out of 36 animals dying between the 12th and 25th

day of cortisone treatment; in the other two groups it was normal.

[The dose of cortisone in the high-dosage group (50 mg. per kg. body weight) is extremely high and must be regarded as a possible source of error in the results because of its indirect effects.] *H. Herxheimer*

910. **Histological Changes in the Gastric Mucosa during Digestion and Their Relationship to Mucosal Growth**
R. GRANT, M. I. GROSSMAN, and A. C. IVY. *Gastroenterology* [*Gastroenterology*] **25**, 218–231, Oct., 1953. 19 figs., 23 refs.

The histological changes in the gastric mucosa during digestion were studied in a series of experiments at the University of Illinois, Chicago. Dogs, cats, and kittens were given raw minced meat and 2 to 7 hours later small pieces of gastric mucosa were taken from the greater and lesser curvatures of the body and from the pyloric antrum. A layer of secretion lying on the mucosal surface was observed in many areas, which varied in depth, consistency, cellular content, and reaction to mucicarmine. During digestion the changes in the mucosa itself included widening of crypts, appearance of gaps in surface epithelium, reduction of depth in certain areas, and increased mitotic activity. The general picture of cellular loss and mucosal changes appeared to be similar to that produced by mild irritants. *R. A. Gregory*

911. **The Resorption of Amyloid under Experimental Conditions**
G. W. RICHTER. *American Journal of Pathology* [*Amer. J. Path.*] **30**, 239–261, March–April, 1954. 15 figs., 18 refs.

The experimental work described in this paper from the New York Hospital–Cornell Medical Center was undertaken to demonstrate that amyloid deposits produced in the spleen of the rabbit by injections of sodium ribose nucleate are resorbed. A subcutaneous injection of 10 ml. of 5% sodium ribose nucleate was given to each of 8 rabbits 5 times a week. After 6 months laparotomy was performed and a portion of the spleen was removed for biopsy. No further injections were given and the animals were killed 3 to 5 weeks later, when blocks of tissue were removed from the main organs. Biopsy and post-mortem material was also taken from 4 control animals. The tissues were fixed in Zenker's fluid and 10% formalin. Paraffin sections were stained with haematoxylin and eosin, Congo red, cresyl violet, and by the periodic-acid–Schiff procedure. Sections of kidney were also stained by the periodic-acid–Schiff–colloidal-iron method of Rinehart and Abul-Haj.

Examination of biopsy specimens from the spleen of the test animals showed conspicuous amyloid deposits; in 3 of the animals there were also foreign-body giant cells. Post-mortem examination revealed that in 4 of the test animals the amyloid deposits had completely disappeared and in 4 they were considerably reduced in amount. Large mononuclear cells were seen in the areas where there had previously been amyloid deposits. Extensive plasmacytosis was also observed in the spleen and lymph nodes of these animals. No definite evidence of resorption of amyloid was found in the kidneys.
A. Wynn Williams

CHEMICAL PATHOLOGY

912. **Chemical Changes in the Human Brain with Increasing Age.** (Die chemischen Alternswandlungen des menschlichen Gehirnes)
M. BÜRGER. *Zeitschrift für Altersforschung* [*Z. Altersforsch.*] **8**, 1–19, March, 1954. 4 figs., 26 refs.

In a study carried out by the author at Leipzig University Medical Clinic the chemical composition of brain substance was determined for each decade from 10 to 90 years of age, a total of 240 brains, equal numbers from each decade and sex, being examined. The brain loses about 100 g. in weight in the course of an average lifetime, and at all ages the female brain weighs less than the male. The techniques of preparation of the post-mortem material and of the various estimations carried out are described.

The calorific value of desiccated brain varied between 6,800 and 7,000 cal. per g. in both sexes, reaching a maximum at 51 to 60 years of age. It was about 5,400 cal. per g. for the dry, fat-free residue, also maximum at 51 to 60 years, and about 8,000 cal. per g. for total lipid, the maximum being at 21 to 30 years for both sexes, from which period there was a small but steady decline with increasing age.

The total lipid content formed 53 to 60% of the dry weight and varied little with age; at all ages the lipid content of the male brain exceeded that of the female by 3 to 5%. Total steroids formed about 25% of the total lipids and showed little change with age or sex. Cholesterol formed about 20%, reaching a maximum in males at 31 to 40 years and in females at 21 to 30 years, but the age and sex differences were small. Phosphatides contributed 36 to 40% of the total lipids, with no sex difference, but showed a fall with increasing age. Plasmalogen in both sexes showed a steady rise up to 70 years of age, then a fall. The phosphatides were fractionated with methanolic silver nitrate at *p*H 4 to 5. In both sexes, there was a marked rise in the amount of precipitate after the age of 70 years. Cerebroside varied irregularly with age and sex, forming from 13 to 18% of the total lipid content. Sulphatide, forming 6 to 8% of the total lipids, was higher in the female than in the male at all ages, the female brain showing a steady increase with increasing age, while a similar, but less marked, increase occurred in the male. Ganglioside, determined as neuraminic acid, varied from 1·4 to 3·5% of the total lipid, differed little in males and females, and was higher in the older decades.

Dry, lipid-free brain substance was also analysed for sulphur, phosphorus, and nitrogen content. Sulphur formed about 1%, and at all ages was higher in females than in males, reaching a maximum in both sexes at 41 to 50 years of age. Phosphorus, varying from 1·1 to 1·5%, also reached a maximum in this decade; it showed no regular sex difference. Nitrogen varied from 13 to 14%, and showed little age or sex difference.
M. Lubran

913. **Glucose and Acetone as Sources of Error in Plasma Creatinine Determinations.**
H. N. HAUGEN. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] **6**, 17–21, 1954. 10 refs.

The effect of the presence of glucose and acetone on the estimation of creatinine in aqueous solutions and in plasma by the Jaffé (alkaline picrate) reaction was studied at Ullevål Hospital, Oslo. It was found that both glucose and acetone contributed to the colour given by creatinine, with the result that false high creatinine levels were recorded, these being still higher if the reading was delayed. Most of this " pseudocreatinine " could be removed by shaking the aqueous solution or the plasma with Lloyd's reagent. In the author's view the time factor is important, and in plasma the result should be recorded after 10 minutes. The concentrations of glucose used varied from 350 to 900 mg. per 100 ml. and of acetone from 20 to 60 mg. per 100 ml. At normal blood sugar levels the creatinine value was not interfered with, but in diabetic patients this interference should be taken into account. *Walter H. H. Merivale*

914. **A Modification of the Dye-dilution Method for Serial Estimations of Plasma Volume**
A. A. PLENTL and M. M. GELFAND. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **98**, 485–493, April, 1954. 3 figs., 14 refs.

In this paper from the Presbyterian Hospital (Columbia University), New York, the authors describe a modification of the dye dilution method for the more accurate determination of plasma volume, commenting that with the increasing use of massive blood transfusions an exact knowledge of the volume of circulating blood is important in order to guard against over- or under-transfusion.

The aim of the modification is to increase accuracy in measuring the amount of dye administered, and a simple apparatus, embodying a burette, enabling this to be done is described. A further aid to accuracy is the use of a dye solution much more dilute than that generally employed hitherto. This was prepared by adding 5 ml. of a 0·3% stock solution of azovan (Evans) blue to 20 or 30 ml. of normal saline. Only a fraction of the test solution, the concentration of which ranged from 0·04 to 0·06%, was used for the estimation of plasma volume and an aliquot was set aside for an accurate analysis of its dye content. This was accomplished by a volumetric dilution in the ratio of 1:250 or 1:125, using normal saline as diluent, and reading the colour intensity against pure water or saline. For the determination of the optical density the Beckman spectrophotometer was used at an arbitrarily chosen wave length of 620 millimicrons. Because of the reduction in the amount of dye used (3 to 4 mg. instead of the usual 15 to 20 mg.) two, three, or four estimations of plasma volume can be carried out in close succession without risk of causing objectionable discoloration of the patient's skin.

The authors also confirmed that the " cat effect " is not demonstrable in the human subject. This phenomenon was first described by Cruickshank and Whitfield (*J. Physiol.* (*Lond.*), 1945, **104**, 52), who presented evidence showing that in the cat a significant portion of the dose of dye injected is phagocytized by the reticulo-endothelial system and thus immobilized. This would result in erroneously high values for the dilution of the dye and consequently for the plasma volume. (The phenomenon has not been demonstrated in other experimental animals.) A number of examples of the application of the authors' method for serial blood volume determinations during major operations are presented. *E. Forrai*

915. **A Clinical Method for Determination of Plasma Galactose in Tolerance Tests**
N. TYGSTRUP, K. WINKLER, E. LUND, and H. C. ENGELL. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] **6**, 43–48, 1954. 4 figs., 16 refs.

916. **Assay of Plasma Insulin Activity by the Rat-diaphragm Method**
P. J. RANDLE. *British Medical Journal* [*Brit. med. J.*] **1**, 1237–1240, May 29, 1954. 2 figs., 17 refs.

A method for the accurate determination of the insulin activity of the plasma has been developed as a modification of that described by Groen *et al.* (*J. clin. Invest.*, 1952, **31**, 97), which is based on the fact that the isolated rat hemidiaphragm will take up glucose from a glucose–buffer solution in which it is suspended, and that this uptake can be measurably increased by adding insulin, or plasma with insulin activity. The responsiveness of the rat hemidiaphragm in terms of glucose uptake to increasing doses of insulin was first confirmed and plotted. Blood was then obtained from healthy subjects 2½ hours after the ingestion of 50 g. of glucose orally, and the plasma was shown to have an insulin activity of between 12·4 and 13·5 milliunits per ml. As the author points out, this figure is higher than that of other workers using the same method, and considerably higher than the figure of 0·34 milliunit per ml. obtained by Bornstein and Lawrence (*Brit. med. J.*, 1951, **2**, 1541; *Abstracts of World Medicine*, 1952, **11**, 256) by assay on alloxan-diabetic, hypophysectomized, adrenalectomized (A.D.H.A.) rats.

This human plasma, shown to have an insulin activity of 13 milliunits per ml. by the rat-diaphragm method, was found to have no effect on the blood sugar of alloxan-diabetic hypophysectomized (A.D.H.) rats, although these animals showed a lowered blood sugar level after the injection of 2 milliunits of crystalline insulin. The author confirmed the fact that cysteine, when incubated with plasma, inhibited the insulin activity of such plasma. He considers that the specificity and sensitivity of the rat hemidiaphragm may differ in various strains, and that this could account for discrepancies in the results of different workers. The marked difference in results between the rat diaphragm method and the A.D.H.A.-rat method is considered to be due to the presence of insulin antagonists in the plasma which are effective *in vivo*, but not with the isolated diaphragm *in vitro*.

It is clear from the author's carefully conducted experiments, and from the work of others, that insulin activity

of human plasma as measured by existing techniques is not a measure of insulin content, and the author stresses the importance of further elucidation of this problem.

[Readers are advised to consult the original article for experimental detail and for the statistical methods employed in analysis of the results.]

J. N. Harris-Jones

917. **Colloid Osmotic Pressures of Serum Proteins in Nephrosis and Cirrhosis: Relations to Electrophoretic Distributions and Average Molecular Weights**

S. H. ARMSTRONG, R. M. KARK, J. A. SCHOENBERGER, J. SHATKIN, and R. SIGHTS. *Journal of Clinical Investigation* [*J. clin. Invest.*] **33**, 297–310, March, 1954. 10 figs., 41 refs.

At the University of Illinois College of Medicine, Chicago, the authors set out to determine whether the colloid osmotic pressure of the plasma, a knowledge of which is valuable in the treatment of oedema, could be accurately predicted from the total protein and albumin and globulin levels. Direct osmotic-pressure measurements by means of the Hepp osmometer and determinations of protein nitrogen level, Tiselius electrophoretic distribution of protein components, and protein specific refractive increment were therefore made on samples of serum from nephrotic children undergoing spontaneous diuresis induced by measles, the object being to test the finding of Scatchard *et al.* (*J. clin. Invest.*, 1944, **23**, 458) that the osmotic pressure of normal pooled plasma is correlated with the albumin and globulin levels.

The correlation was satisfactory at low osmotic pressures, but in the intermediate range the predicted pressures were too low. Osmotic pressures calculated from uncorrected electrophoretic measurements on 27 samples of serum and 19 of ascitic fluid from cirrhotic patients were similarly low; and the osmotic pressure of serial samples of serum from a patient with severe cirrhosis showing clinical improvement actually doubled without significant changes in the electrophoretic components of the serum. Examination of the relation of osmotic pressure to protein concentration values in comparison with the protein concentration curves from waterlogged cirrhotic patients gave no evidence of large non-lipid-bearing globulin molecules or of dissociation of larger molecules with dilution. Also, the average molecular weights calculated from normal electrophoretic albumin and gamma globulin values were only slightly greater than the measured ones. Proteins in nephrotic serum had high average molecular weights (160,000 to 830,000), which varied with the stage of the syndrome; the aggregates did not dissociate on dilution. The curves neither confirmed nor excluded the possible existence of proteins with unusual osmotic properties, as suggested by measurements on patients with severe hypoproteinaemia and oedema.

The authors conclude that in cases of severe hypoproteinaemia, in which accurate osmotic values are required, the total protein level and distribution of albumin and globulin are not a reliable guide, and the plasma osmotic pressure should therefore be measured directly.

J. E. Page

918. **Paper Micro-electrophoresis with Toluidine Blue and its Practical Application.** (La micro-électrophorèse sur papier avec le bleu de toluidine et ses applications pratiques)

E. BENHAMOU, J. PUGLIÈSE, J. C. CHICHE, and P. AMOUCH. *Presse médicale* [*Presse méd.*] **62**, 651, April 28, 1954. 6 figs., 9 refs.

The authors describe a method for the separation of blood polysaccharides by micro-electrophoresis on paper stained with toluidine blue either before or after oxidation with periodic acid and bromine water. No details of the electrophoretic separation or photo-electric estimation of the polysaccharides are given but the technique of staining is as follows: the paper is first allowed to soak for 30 minutes in a 0·1% solution of toluidine blue, then rinsed in running water, treated with 4% ammonium molybdate solution, and dried at 100° C.; this procedure gives a measure of the acid polysaccharides. When oxidation is carried out first the strip of paper is immersed for 15 minutes in a solution of periodic acid, transferred for a further 15 minutes to bromine water, rinsed in plain water, and then treated with toluidine blue solution as before. By this technique the 1:2-glycol groups of neutral polysaccharides are oxidized to carboxylic acid groups and the final colour gives a measure of both the neutral and acid polysaccharides.

The method has been applied to blood samples from normal subjects and from patients suffering from conditions such as pulmonary tuberculosis, rheumatic fever, amyloidosis, nephrosis, nephritis, diabetes mellitus, and hepatic cirrhosis. [The original article should be consulted for the coloured illustrations which it contains of the various electrophoretograms obtained.] The papers were also stained for proteins and lipids and with periodic-acid–Schiff as well as with the toluidine blue before and after oxidation.

M. J. H. Smith

919. **Chemical Screening Methods for the Diagnosis of Pheochromocytoma. I. Norepinephrine and Epinephrine in Human Urine**

M. GOLDENBERG, I. SERLIN, T. EDWARDS, and M. M. RAPPORT. *American Journal of Medicine* [*Amer. J. Med.*] **16**, 310–327, March, 1954. 2 figs., 31 refs.

At Columbia University, New York, a comparison was made of the relative value of chemical methods over the usual biological methods for the routine investigation of urinary catechol amines in the diagnosis of phaeochromocytoma.

The first step was to obtain urine extracts by adsorption of the amines on precipitated aluminium hydroxide, this being followed by elution, desalting, and concentration *in vacuo*. The extracts were then tested by their effect on the blood pressure of the cat, the results being expressed in noradrenaline equivalents. In 13 normotensive subjects and 35 patients with essential hypertension the noradrenaline equivalents never exceeded 100 μg. per day. In 16 cases of phaeochromocytoma this value was always far higher, ranging from 190 to 2,700 μg. per day. One of this last group gave false negative responses to benzodioxane, "regitine", and histamine. Secondly, the urine extracts were

developed by paper chromatography, using water-saturated phenol. Of the 16 patients with phaeochromocytoma, 15 gave positive findings by paper chromatography (that is, more than 20 μg. per ml. of urine extract). Thirdly, the quantitative estimation of adrenaline and noradrenaline in the urine extracts was carried out by a modification of the photofluorometric method of Lund (*Acta pharmacol.*, 1949, **5**, 231), which involves the formation of fluorescent oxidation products, adrenolutine and noradrenolutine. Lastly, the urine extract (concentrated 5 times) was chromatographed in the usual way, using butanol–acetic acid–water as developer, and the eluates of the separated adrenaline and noradrenaline were determined quantitatively by a fluorimetric procedure after oxidation by manganese dioxide, sodium hydroxide, and ascorbic acid solution. Recoveries of standard amounts of the synthetic materials by this method ranged from 85 to 108%. In 4 out of 5 cases of phaeochromocytoma this last chemical method yielded results at least 30% higher than those found by bio-assay. [The various steps are fully described and the reader should consult the original paper for further details.]

The authors suggest that a rapid screening procedure for urinary extracts, involving adsorption on an alumina column, elution with acetic acid, and fluorimetric measurements, is worthy of consideration for mass screening of hypertensive patients. When positive results are obtained the more reliable diagnostic test for phaeochromocytoma by the longer and specific method of photofluorimetric evaluation of urinary extracts should be carried out.

Since the urinary excretion in 10 cases of Addison's disease was within normal limits, the authors state that the source of the noradrenaline in the urine is probably the sympathetic nervous system. This statement is supported by the fact that the lowest urinary excretion values were found in cases subjected to thoracolumbar sympathectomy. It is probably true that the amount of noradrenaline in the urine represents only a small fraction (up to 4%) of the total amount secreted by the tumour in cases of phaeochromocytoma.

G. B. West

920. **The Clinical Significance of the Diastase Content of Blood and Urine in Mumps.** (Die klinische Bedeutung der Diastasebestimmung in Blut und Harn bei der Parotitis epidemica)
E. HAUSMANN. *Archiv für Kinderheilkunde* [*Arch. Kinderheilk.*] **148**, 135–146, 1954. 1 fig., 27 refs.

At the Wilheminen Hospital, Vienna, the serum and urinary diastase content was determined in 65 cases of mumps, all but 6 of the patients being children. In 55 (85%) of the cases the diastase values were increased during the first 11 days of the illness, although in 21% of them the increase was found only in the serum or only in the urine, and in a few cases only after repeated examination. As the diastase levels fluctuate considerably the author suggests that for diagnostic purposes they should be estimated repeatedly, as a single estimation will give normal values in 15% of cases. Orchitis alone had no effect on the diastase level. *H. Lehmann*

921. **Amino-aciduria in March Haemoglobinuria**
C. M. B. PARE and M. SANDLER. *Lancet* [*Lancet*] **1**, 702–704, April 3, 1954. 19 refs.

The authors report, from Shorncliffe Military Hospital, Kent, the coincidental finding of amino-aciduria in 12 patients admitted to the hospital with march haemoglobinuria, a condition which appears, usually in young men, after marching or other vigorous exercise in the upright position, and of which the most striking characteristic is the passing of urine of a deep port-wine colour. By means of a 2-dimensional chromatographic technique on filter paper and the use of conventional solvent mixtures, cystine was identified in the urine of all the patients and β-amino-*iso*butyric acid in the urine in 11 cases, although in 2 of these the amount was small. In 2 cases there was "generalized amino-aciduria". The 2 patients with the highest urinary cystine excretion showed chromatographic patterns consistent with heterozygous cystinuria.

The authors conclude that the reabsorption of cystine, β-amino-*iso*butyric acid, and haemoglobin occurs in the same or adjacent sections of the renal tubule, and that the low renal threshold for haemoglobin in march haemoglobinuria is a non-specific tubular defect.

Walter H. H. Merivale

922. **Determination of Function of the Individual Kidney**
T. E. NESBITT. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **71**, 407–411, April, 1954. 7 refs.

The need for determining the functional capacity of each kidney separately frequently confronts the clinician, and until recently no entirely satisfactory method has been available. At the University of Michigan, Ann Arbor, the author has measured the functional capacity of the individual kidney by utilizing the 24-hour endogenous creatinine test for total renal function. Patients on whom retrograde pyelograms were to be performed were maintained on a meat-free diet for 48 hours to exclude sources of exogenous creatinine, and a 24-hour creatinine clearance test was performed to serve as a control for the individual estimations. Urine was collected for a 30-minute period from each kidney by ureteric catheter, and at the same time venous blood samples were taken for determination of the serum creatinine level. Thus the 30-minute creatinine clearance by each kidney could be calculated, from which the 24-hour clearance could be obtained by extrapolation and compared with the result of the 24-hour creatinine clearance test. Information was thus obtained on the function of each kidney.

The results of the performance of this test on 5 patients with known or suspected renal disease are discussed. It is claimed that the test is simpler to perform than the urea clearance test and is sufficiently accurate for clinical work. The test is recommended for use in cases of known or suspected renal dysfunction in which operation is contemplated, when a knowledge of the type and extent of the lesion is important in order to conserve as much functional renal tissue as possible. When no loss of renal function is suspected the phenolsulphonphthalein test should be used for routine testing. The author's

technique is described, and the necessity for using a sufficiently large catheter and ensuring that its tip is lying at or within the renal pelvis is pointed out.

J. E. Page

HAEMATOLOGY

923. **Significance of Nucleated Red Blood Cells in Peripheral Blood. Analysis of 1,496 Cases**
S. O. SCHWARTZ and F. STANSBURY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **154,** 1339–1340, April 17, 1954. 5 refs.

The records of 1,496 cases seen at Cook County Hospital, Chicago, between 1941 and 1951 in which nucleated erythrocytes were found in the peripheral blood have been reviewed to determine the prognostic significance of this finding.

Blood disorders commonly associated with erythroblastosis are haemorrhagic anaemia, pernicious anaemia, leukaemia, and haemolytic anaemia. The number of cases of each of these conditions in the present series was as follows (mortality in brackets): haemorrhage 361 (36%); pernicious anaemia 270 (29%); leukaemia and related conditions 154 (76%); haemolytic anaemia 86 (20%). The third and fourth largest groups in this whole series were, however, carcinoma (224 cases, mortality 61%) and cardiac disease (195 cases, mortality 66%). Infections (115 cases, mortality 57%) and miscellaneous conditions such as cerebral vascular disease and diabetes (91 cases, mortality 50%) accounted for the remainder. The authors conclude that the presence of nucleated erythrocytes in the peripheral blood indicates that the prognosis is poor not only in cases of blood dyscrasia, but also in cases of carcinoma, cardiac disease, and infection, particularly when accompanied by anoxia. The finding is of least prognostic significance in cases of haemolytic anaemia, haemorrhage, and pernicious anaemia.

[No reference is made to the frequency of this finding in the conditions mentioned or to the mortality among those in which it was not present.]

Nigel Compston

924. **The Bone Marrow and Liver in Iron-deficiency Anemia. A Histopathologic Study of Sections with Special Reference to the Stainable Iron Content**
E. BEUTLER, W. DRENNAN, and M. BLOCK. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **43,** 427–439, March, 1954. 9 figs., 31 refs.

A study of the bone marrow and the liver in iron-deficiency anaemia is described in this paper from the University of Chicago. Marrow biopsy was carried out on 23 patients with iron-deficiency anaemia and 12 healthy subjects. Smears were prepared, Wright's stain being used, and fragments of the specimen were fixed in Zenker's formol, dehydrated, embedded in nitrocellulose, and sectioned at 6 μ. From each specimen some slides were stained with haematoxylin–eosin–azure-blue, and others were stained for iron by placing them in a fresh mixture of 1 part of 2% potassium ferrocyanide and 2 parts of 1% hydrochloric acid for half an hour. Additionally, all negative specimens were stained for 10 minutes in a 1:1 mixture of 4% hydrochloric acid and 4% potassium ferrocyanide heated to 56° C.

The bone marrow of the patients with iron-deficiency anaemia was generally more erythroblastic and more cellular than that of the controls, but the overlap in the two groups was very large. No correlation was observed between the degree of anaemia and the percentage of erythroblasts in the smears or sections. Administration of iron generally produced increased erythroblastic hyperplasia, and the magnitude of the response was roughly proportional to the severity of the anaemia. Stainable iron appeared in the marrow very soon after intravenous administration of iron; it appeared more slowly or not at all after iron was given by mouth.

Examination of needle-biopsy specimens of the liver of 2 of the patients did not reveal any abnormality. After intravenous administration of saccharated oxide of iron there was deposition of iron exclusively in the littoral cells of the sinusoids.

In view of the slow re-accumulation of storage iron after oral administration the authors emphasize the importance of continuing this method of treatment for some time after the blood picture has become normal.

D. G. Adamson

925. **The Erythrocyte Sedimentation Rate and the Plasma Viscosity**
R. D. EASTHAM. *Journal of Clinical Pathology* [*J. clin. Path.*] **7,** 164–167, May, 1954. 4 figs., 14 refs.

926. **Sideroblasts. A Study of Stainable Nonhemoglobin Iron in Marrow Normoblasts**
E. KAPLAN, W. W. ZUELZER, and C. MOURIQUAND. *Blood* [*Blood*] **9,** 203–213, March, 1954. 7 figs., 11 refs.

Sideroblasts are normoblasts in which iron-staining granules can be demonstrated. The authors, at the Children's Hospital (Wayne University), Detroit, studied the incidence of these cells in the bone marrow of healthy children and children suffering from different forms of anaemia.

Sideroblasts were found in the bone marrow of all the healthy children, constituting between 20 and 90% of the normoblasts. The number of iron-staining inclusions varied from 2 to 30 per cell. In anaemia associated with renal disease and infection and in aplastic anaemia the percentage of sideroblasts was normal. In haemolytic anaemia, including thalassaemia minor, and in megaloblastic anaemia the proportion of sideroblasts was somewhat higher than that observed in normal bone marrow. In iron-deficiency anaemia, however, a marked reduction in the percentage of sideroblasts was observed. As might be expected in this condition considerable correlation was found between the serum iron level and the proportion of sideroblasts in the marrow, both values tending to be low. Administration of iron intravenously produced a rapid increase in the number of sideroblasts. Tissue culture, in an iron-containing medium, of the marrow from a patient with iron-deficiency anaemia revealed a rise in the number of sideroblasts in the specimen.

Nigel Compston

MORBID ANATOMY AND CYTOLOGY

927. **Perivascular Encephalolysis. Histopathology and Pathogenesis**
M. T. MOORE. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **71**, 344–357, March, 1954. 11 figs., 26 refs.

The pathology of perivascular encephalolysis is exemplified by a detailed account of 2 cases from the Hospital of the University of Pennsylvania, Philadelphia, in both of which there was an underlying metabolic disorder, diabetes mellitus. The essential lesion in the brain consisted of perivascular demyelination around the smaller vessels throughout the brain, but especially in the cerebral cortex and subcortex, accompanied by perivascular liquefaction necrosis with lysis of the perivascular tissue. Four stages in the development of the lesion were recognized: (1) a hyaline–fibrinoid degeneration of the vessel with obliteration of the perivascular space by glial proliferation, particularly of the oligodendroglia; (2) an increased glial reaction with beginning lysis of the surrounding tissues; (3) disappearance of the neuroglial elements, with an increase in the amount of tissue lysis and liquefaction necrosis; and (4) complete perivascular cystic necrosis. [Excellent illustrations of these four stages are given in the text.]

The pathogenesis of the lesion is discussed at length. The author considers that the factors which influence the morbid process are: (1) structural changes in the small vessels of the brain (due to atherosclerosis in both the patients whose cases are described); (2) vulnerability of the tissues due to a " systemic " factor (in these cases, diabetes mellitus); (3) accumulation of catabolites in the perivascular space (resulting in these cases mainly from faulty metabolism due to the diabetes and a consequent decrease in cerebral oxygen consumption); and (4) imbalance of the myelin–oligodendroglial enzyme system, which favours the formation of an encephalolytic substance (here produced by relative cerebral anoxia). All these factors were present in both the cases described, but the author stresses the importance of the disordered cerebral tissue metabolism due to the diabetes, and especially of the decreased oxygen consumption of the brain. *Ruby O. Stern*

928. **Basement Membrane Changes in Chronic Thyroiditis and Other Thyroid Diseases**
S. C. SOMMERS and W. A. MEISSNER. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **24**, 434–440, April, 1954. 10 figs., 14 refs.

The characteristics and extent of basement membrane in the thyroid gland of healthy subjects and of patients with thyroid disease, especially thyroiditis, were investigated at the Cancer Research Institute and New England Deaconess Hospital, Boston. Sections of thyroid tissue were stained by the method of McManus and Mowry (sulphuric acid–haematoxylin). Specimens from patients with chronic thyroiditis revealed thinning and generalized weakness of the basement membrane. Similar changes were observed in the salivary glands in 2 cases of Mikulicz's disease, and the authors note that Hashimoto discussed the relationship between the latter and struma lymphomatosus. They state that tissues derived from the branchial clefts are peculiarly susceptible to this form of degeneration of the basement membrane.
A. C. Lendrum

929. **The Morbid Histology and Pathogenesis of Cerebral Arterial Aneurysms.** (Histopathologie et pathogénie des anévrysmes artériels cérébraux)
A. E. WALKER and G. E. ALLÈGRE. *Revue neurologique* [*Rev. neurol.* (*Paris*)] **89**, 477–490, 1953 (received May, 1954). 6 figs., 28 refs.

The histological findings in 39 cases of cerebral arterial aneurysm are reported, from which it is concluded that localized vascular degenerative changes—especially proliferative changes in the intima—may be more important in pathogenesis than is generally supposed.

The patients' ages ranged from 29 to 72, with a mean of 42·7 years. In all but 5 cases death could be directly attributed to the presence of the aneurysm or to its attempted removal. Generalized hypertension was present in 18 cases, generalized atherosclerosis in 21, and various overt congenital anomalies (such as polycystic kidney or vertebral haemangioma) in 9. Frank sclerosis of the vessels at the base of the brain was observed in 13 cases, and foci of cerebral softening in 4.

The presenting signs were those of meningeal haemorrhage in 29 cases, but surgical trauma may have been responsible for the haemorrhage in one of these. In most instances the haemorrhage was not limited to the convexities of the brain but had also entered the basal cisterns. In nearly half the cases there was evidence of intracerebral bleeding, and in one-third of these practically a whole hemisphere had been destroyed.

The commonest site for aneurysmal rupture was the supraclinoid portion of the internal carotid artery (16 cases), the next commonest being the proximal part of the anterior cerebral artery (12 cases); the posterior cerebral artery was affected in 2 cases, and the posterior communicating, basilar, and vertebral arteries accounted for one each. Coexistent intact aneurysms at various sites were also seen.

Only 2 of the aneurysms were fusiform in shape, all the remainder being saccular. Their diameter varied from 2 mm. to 5 cm., most often being about 1 cm.

Histological examination revealed marked atheromatous change in the immediate vicinity of the aneurysm in 25 of the 29 specimens studied. In all but one, at the junction between the sac and the vessel, there was extensive proliferation which appeared to have invaded the neighbouring elastic coat, distorting it or even causing it to disintegrate. The wall of the sac itself was mainly composed of hyaline connective tissue, with a few fragments of elastic tissue and occasional smooth-muscle fibres. Atheromatous plaques were common.

It is concluded that while congenital factors undoubtedly play a part, there is probably no single causal mechanism to account for the formation of cerebral arterial aneurysms; it is stressed that the various hypotheses which have been propounded are by no means mutually exclusive. *Adrian V. Adams*

930. **Intracranial Metastasis from Carcinoma of the Lung**
B. HALPERT, W. S. FIELDS, and M. E. DE BAKEY. *Surgery* [*Surgery*] **35**, 346–349, March, 1954. 7 refs.

To determine the frequency of intracranial metastases from carcinoma of the lung, the necropsy findings in 100 cases of this disease at the Veterans Administration Hospital, Houston, Texas, were studied. In 92 of these cases the brain was examined. All the patients were males, and 76 were over 50 years of age. Intracranial metastases were found in 30 of the 92 cases in which the brain was examined, but there was no correlation between the frequency of metastases and the cell type of lung tumour. In 10 of these 30 there had been clinical symptoms of involvement of the central nervous system. The incidence of metastasis to the brain was exceeded only by that to regional lymph nodes, liver, and adrenal glands. *G. Calcutt*

931. **Anatomical and Histological Findings after Lumbar Intrathecal Injections.** (Anatomische und histologische Befunde nach lumbalen Injektionen)
A. RIMPAU. *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* [*Virchows Arch. path. Anat.*] **325**, 179–188, 1954. 6 figs., 42 refs.

At Heidberg General Hospital, Hamburg, the author examined the lumbar region of 3 patients with tuberculous meningitis who had died after intensive intrathecal therapy. The subcutaneous tissues showed necrotic areas, scars, and haemorrhages. The dura displayed groups of incompletely closed or healed puncture openings, while the inner surface of the dura, as well as the leptomeninges, exhibited small, circumscribed granulomata with foreign-body giant-cells encasing birefractile bodies of round or rectangular shape and often displaying frayed ends. Similar granulomata were also present in the subcutaneous tissue. In another case examined the lesions observed were of a tuberculous nature. The author regards the foreign bodies found as fibres of plant origin, possibly adherent to the lumbar-puncture needles and introduced into the tissues at the time of the lumbar puncture. The literature is reviewed. *R. Salm*

932. **The Pathology of Bronchial Asthma.** (Zur Pathologie des Asthma bronchiale)
F. GLOOR. *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* [*Virchows Arch. path. Anat.*] **325**, 189–210, 1954. 6 figs., bibliography.

In this paper from the University of Basle the author describes the post-mortem findings in the lungs of 7 patients dying during an asthmatic attack, of 4 asthmatic patients dying from an intercurrent illness, and of a control series of 20 patients who died from severe purulent bronchitis and had shown clinically some " asthmoid " symptoms.

In the first two groups the lungs were inflated, and both smaller and larger bronchi were filled with viscid mucus, the medium-sized bronchi, measuring 1 to 4 mm. in diameter, being mainly and characteristically affected. The principal changes observed were: (1) filling of the bronchial lumina with viscid mucus, frequently displaying a spiral twist, and showing an admixture of bronchial epithelial cells and eosinophil leucocytes; (2) partial replacement of the bronchial columnar cells by mucus-producing goblet cells; (3) infiltration of the congested bronchial walls with inflammatory cells, among which eosinophils were predominant; (4) considerable thickening of the basal membranes (up to 25 μ); and (5) hyperplasia of the bronchial mucous glands. Subepithelial elastic cushions were observed only occasionally, but thickening of the bronchial muscles was seen frequently, mainly in the larger bronchi.

These changes the author interprets as an allergic antigen–antibody reaction confined to the medium-sized bronchi, and he stresses that the features were always present in patients in the first two groups, irrespective of whether death was due directly or indirectly to asthma. As not a single case in the third (control) group exhibited these features, the author regards them as characteristic of asthma. *R. Salm*

933. **Occult Carcinoma of the Major Bronchi**
W. H. WIERMAN, J. R. MCDONALD, and O. T. CLAGETT. *Surgery* [*Surgery*] **35**, 335–345, March, 1954. 5 figs., 21 refs.

At the Mayo Clinic resection was carried out in 5 cases of squamous-cell carcinoma of the major bronchi, and in this paper these cases are described in detail. In no case was there any apparent gross tumour formation, but in 4 there were malignant cells in the sputum. Bronchoscopy in 3 cases revealed a roughened area on the mucosa, and biopsy examination of this area disclosed a tumour. It is pointed out that an epidermoid bronchogenic carcinoma can occur as a non-projecting tumour, but that under these conditions the normal longitudinal furrowing of the bronchus is obliterated. Such an area of morphological change can be detected by bronchoscopy and should be subjected to biopsy.

G. Calcutt

934. **Findings in Interstitial Plasma-cell Pneumonia.** (Befunde bei interstitieller plasmazellulärer Pneumonie)
H. DIEKMANN, E. LINDNER, and E. STOPKA. *Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie* [*Beitr. path. Anat.*] **114**, 48–64, 1954. 8 figs., 29 refs.

A series of 32 cases of interstitial plasma-cell pneumonia in infants were examined post mortem at the Düsseldorf Academy of Medicine. *Pneumocystis carinii*, the protozoon described as occurring in the lungs in this form of pneumonia by Vanek and Jirovec, was found in all cases and in none of the 28 control subjects with other diseases. A method for enrichment of the protozoa in suspensions of teased lung tissue is described. Such enriched suspensions were examined by phase-contrast and electron microscopy, valuable details of the cytomorphology of the parasites being obtained. It is concluded that interstitial plasma-cell pneumonia is a disease *sui generis*, quite distinct from any other form of interstitial pneumonia.

[Outside the European continent only one case of this

disease has been reported (Baar, *J. clin. Path.*, 1954, **7**, 169), and in this case also the presence of *Pneumocystis carinii* was confirmed.] *H. S. Baar*

935. **Some Morphological Findings Supporting the Idea of Nervism in Pathology.** (Некоторые морфологические данные, развивающие идею нервизма в патологии)
V. K. Zhgenti. *Архив Патологии* [*Arkh. Patol.*] **16**, 3–13, Jan.–March, 1954. 8 figs., 12 refs.

The author reviews the findings of Soviet workers which support the suggestion that the development of local pathological processes is related to the functional state of the nerves supplying the tissues affected, which may be reflected in the morphology of the afferent and efferent nerve fibres and their endings. Changes found in several organs are described—for example, in the larynx of patients with pulmonary tuberculosis with and without local laryngeal involvement, and in the genital organs of men with pulmonary tuberculosis with and without local genital disease. Similar studies of changes in the meninges are reported, and also of the effect of streptomycin therapy on the structural changes in nerve fibres. It is stated that tuberculous lesions in organs other than the lungs in cases of pulmonary tuberculosis are preceded by morphological changes in the nerve fibres, and it is suggested that some trophic disturbance is necessary to enable the tubercle bacillus to gain a foothold in the tissues, with subsequent development of local disease.

Similar findings are described in the nerve fibres of the endocardium in cases of endocarditis and in the nerve endings in tumours and their metastases.

L. Crome

936. **The Chemical Basis of the Silver Impregnation Method.** (О химических основах метода аргирофильной окраски)
G. V. Orlovskaya and A. A. Tustanovskiĭ. *Архив Патологии* [*Arkh. Patol.*] **16**, 13–22, Jan.–March, 1954.

The successive chemical changes involved in the silver impregnation method of Bielschowsky and Foot are discussed, and it is suggested that they depend largely on the SH– and S–S groupings of cysteine and cystine. The denaturation of protein with formalin results in the incomplete participation of these groupings in the reaction, while additional denaturation with urea intensifies the native argyrophilia by the mobilization of some of the "masked" SH– and S–S groupings. *L. Crome*

937. **The Heart Valves in Certain Acute Infections.** (Клапанный аппарат сердца при некоторых острых инфекциях)
B. S. Gusman. *Архив Патологии* [*Arkh. Patol.*] **16**, 42–52, Jan.–March, 1954. 4 figs., 41 refs.

In a series of 41 children dying from dysentery, scarlet fever, diphtheria, influenza, and pneumonia all the valves of the heart showed such non-specific histological changes as oedema, cellular proliferation, accumulation of mucoid material, and alteration in the argyrophil ground substance. In the absence of clinical signs of endocarditis these lesions cannot be regarded as evidence of valvulitis, but they may well be significant in the pathogenesis of cardiac disorders in infectious fevers. The heart valves of rabbits dying after the injection of a lethal dose of dysentery bacilli showed similar changes, and those which survived 2 weeks exhibited some fibrosis. It is therefore possible that some unexplained cases of valvular fibrosis may be the result of a preceding acute general infection.

Blood vessels were found in the valves in 35 cases, thus confirming a previous suggestion that they are a normal histological feature. *L. Crome*

938. **The Role of Intimal Haemorrhage in Coronary Occlusion**
R. A. B. Drury. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **67**, 207–215, Jan., 1954. 7 figs., 30 refs.

In this interesting study carried out at University College Hospital Medical School, London, 55 hearts from subjects dying from coronary arterial disease were examined, together with a control group. Intimal haemorrhage was frequently found in the coronary arteries, and nearly always resulted from haemorrhage into an atheromatous plaque, the overlying endothelium of which had given way. Thrombosis was also found to be associated with rupture of the endothelium over an atheromatous plaque, but was not related to intimal haemorrhage. No evidence was found to support Wartman's view that massive intimal haemorrhage may sometimes cause sudden coronary arterial occlusion. The author believes that although intimal haemorrhage is a common finding in cases of coronary thrombosis, it is one of little importance and should in no way be regarded as a contraindication to anticoagulant therapy.

G. J. Cunningham

939. **Generalized Siderosis with Fibrosis of Liver and Pancreas in Cooley's (Mediterranean) Anaemia**
J. T. Ellis, I. Schulman, and C. H. Smith. *American Journal of Pathology* [*Amer. J. Path.*] **30**, 287–309, March–April, 1954. 8 figs., 29 refs.

The distribution of iron in the tissues in Cooley's anaemia was studied at the New York Hospital–Cornell Medical Center in 6 cases post mortem and in the spleen and liver of 7 patients who underwent splenectomy. The patients' ages ranged from 2 to 27 years. Hepatic siderosis was marked in all but one patient (aged 2 years) and was accompanied by fibrosis in all but this patient and one other (aged 4 years); the fibrosis in 3 cases was severe and comparable with that to be expected in fatal idiopathic haemochromatosis. Siderosis and fibrosis of the pancreas were present in those cases examined post mortem in which the liver was affected, but were less extreme in degree. Siderosis was also found in lymph nodes, spleen, myocardium, renal tubules, thyroid, adrenal, parathyroid, and pituitary glands, gastric and intestinal mucosa, male genitalia, and bronchial glands.

Although the degrees of siderosis and of fibrosis present in the various cases generally ran parallel, definite evidence of a causal relationship between the two was lacking. Nor could the degree of fibrosis be closely correlated with the duration of the disease. The

amount of iron present in the liver often exceeded that which had been given by mouth and by transfusion, suggesting that excessive absorption of iron from the intestine may occur in this condition.

George Discombe

940. **Renal Biopsies in Hypertension**
R. H. HEPTINSTALL. *British Heart Journal* [*Brit. Heart J.*] **16**, 133–141, April, 1954. 9 figs., 11 refs.

The extent to which vascular changes influence the response to sympathectomy in hypertension was studied in biopsy specimens of renal cortex from 50 patients on whom sympathectomy had been performed at St. Mary's Hospital, London. A comparison of these specimens with sections similarly obtained at necropsy indicated that the biopsy specimens were representative of the kidney as a whole, except in cases of chronic pyelonephritis.

Vascular changes were noted in some cases but not in others, although the degree of hypertension was the same in all. This is considered to indicate that the hypertension probably preceded the vascular changes. Arteriolar necrosis was noted only in those cases in which the diastolic blood pressure was highest. The author states that it is possible to obtain as great a reduction in blood pressure in patients with advanced vascular changes as in those less severely affected. *J. B. Wilson*

941. **The Pathology of the Pancreas in the Acute and Chronic Gastrointestinal Disorders of Infancy.** (Zur Pathologie des kindlichen Pankreas bei akuten und chronischen Ernährungsstörungen)
G. SEIFERT. *Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie* [*Beitr. path. Anat.*] **114**, 1–47, 1954. 12 figs., bibliography.

A study was made at the Institute of Pathology of the University of Leipzig of the histopathological changes in the pancreas of 228 children who died of a variety of gastrointestinal diseases, including acute gastroenteritis in 14 cases, chronic and recurrent gastroenteritis in 41, and fibrocystic disease of the pancreas in 9. In acute gastroenteritis serous inflammation of the interstitial tissue of the pancreas and stagnation of secretion in the acini and ducts were found, while in one case this had developed into interstitial purulent pancreatitis, with abscess formation and extensive necrosis. In chronic gastroenteritis there were various degrees of interstitial fibrosis, more or less severe loss of deoxyribose nucleic acid from the nuclei of the secretory cells, and in one-third of the cases cystic dilatations in the duct system. The findings in the 9 cases of cystic fibrosis of the pancreas are described in great detail, the author considering that they support Farber's theory of " polymucoviscidosis ". [The demonstration of an altered pancreatic secretion in fibrocystic disease, attributed here to Farber (1944), was actually recorded by Blackfan and Wolbach in 1933. The development of the cysts, which the author calls " dyschylic ", is rightly described in the text as starting in the acini, but in the schematic drawing the first stage is represented as a dilatation of the ducts. The author describes the microcystic dilatations frequently seen in young infants as dysontogenetic, but gives no reasons for this rather surprising classification.] *H. S. Baar*

942. **Histological Observations on Hepatic Disease in Jamaican Infants and Children.** [In English]
G. BRAS, D. B. JELLIFFE, and K. L. STUART. *Documenta de medicina geographica et tropica* [*Docum. Med. geogr. trop. (Amst.)*] **6**, 43–60, March, 1954. Bibliography.

In this report from the Hospital of the University College of the West Indies, histological details are given of 148 liver biopsies and 12 necropsies performed on 93 Jamaican children suffering from liver disease. The patients were divided into 3 groups according to the main symptoms: (1) kwashiorkor–marasmus (39 cases); (2) veno-occlusive disease (12 cases); and (3) cirrhosis of the liver (8 cases); the remaining 34 cases formed a miscellaneous control group.

The main hepatic change in Group 1 was fatty infiltration. In contrast to the usual findings, liver cell necrosis was not uncommon and pancreatic fibrosis was found in only 2 cases. Aetiology is discussed, and it is considered that pure kwashiorkor results from protein deficiency, and marasmus from severe general malnutrition. In Group 2 the main feature of veno-occlusive disease was endophlebitis of the hepatic veins, with sinusoidal widening, and compression and dissociation of cell cords. The condition may be reversible in the early stages, but a non-portal fibrosis may develop, leading to cirrhosis. This syndrome is common in Jamaica and aetiology and histology are varied. Malnutrition is probably not the sole cause, and toxic factors are believed to be involved. With regard to the cases in Group 3, the evidence suggests that in Jamaica hepatic venous occlusion is a step in the development of many cases of hepatic cirrhosis. The aetiological relationship between kwashiorkor and cirrhosis of the liver is considered and some of the problems it presents are discussed. In the control group, despite obvious malnutrition in many children, pathological hepatic lesions were found in only 2 cases, emphasizing that children can be maintained remarkably well on a very low dietetic level.

J. L. Markson

943. **The Sternoclavicular Articulation in Rheumatic Diseases**
L. SOKOLOFF and I. O. GLEASON. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **24**, 406–414, April, 1954. 7 figs., 12 refs.

The sternoclavicular joint, examined post mortem, was found to be affected by " rheumatic " disorders more frequently and more severely than is generally appreciated. The material was obtained from Bellevue Hospital, New York, from cases of rheumatoid arthritis, gout, infective arthritis, lupus erythematosus, and acute rheumatic disease. For comparison the appearance of the normal sternoclavicular joint and the degenerative changes occurring with age are described. [The number of cases was small, but the illustrations are good proof of the value of examination of this accessible material.]

A. C. Lendrum

Bacteriology

944. **The Growth of Intracellular Tubercle Bacilli in Relation to Their Virulence**
G. B. MACKANESS, N. SMITH, and A. Q. WELLS. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 479–494, April, 1954. 4 figs., 18 refs.

Working at the Sir William Dunn School of Pathology, Oxford, the authors have investigated the growth rates in isolated monocytes of one virulent human strain of *Mycobacterium tuberculosis* (H37Rv), two attenuated strains (R1Rv and H37Ra), and one attenuated bovine strain (B.C.G.), and compared the results with the rates of growth observed in the livers and spleens of albino mice, as measured by a count of viable organisms. A full account of the strains employed is given, as well as a detailed description of the technique and the method of counting.

A quantitative measurement of growth rates by these two methods was found to be possible, and a correlation was found between the results obtained *in vivo* and *in vitro*, the rates of growth varying from strain to strain in the same order in each. There was an initial lag period before growth started *in vitro* as the bacilli adapted themselves to their new situation, the length of this period varying with both the age and virulence of the culture. It is suggested that the virulence of a given strain of tubercle bacillus may be a function of its capacity to survive and multiply intracellularly.

John M. Talbot

945. **The Growth of Tubercle Bacilli in Monocytes from Normal and Vaccinated Rabbits**
G. B. MACKANESS. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 495–504, April, 1954. 2 figs., 13 refs.

As the rabbit is highly resistant to infection with virulent human-type tubercle bacilli, its host cell should be ideal material for the detection of an immune mechanism in the monocyte. In the present study, therefore, carried out at the Sir William Dunn School of Pathology, Oxford, 9-month-old rabbits were injected intravenously with 0·2 ml. of a 7-day " tween "–albumin culture of *Mycobacterium tuberculosis*, strain H37Rv, this dose being repeated 3 months later. Another series of animals were vaccinated with B.C.G., and then given a similar injection of the same culture intravenously. Following the second injection all the vaccinated animals were found to be tuberculin-positive, and were then injected intraperitoneally with liquid paraffin to produce a mononuclear-cell exudate, mononuclear cells also being obtained in a similar manner from normal tuberculin-negative rabbits as a control. All the cells were infected with a 3-week-old culture of a virulent bovine bacillus, a small quantity of streptomycin sufficient to restrain extracellular growth being added. Cultures were examined at 6-hourly intervals for the first 24 hours, and at 12-hourly intervals thereafter.

It was found that the lag phase and subsequent growth rates of bacilli in monocytes from normal and vaccinated rabbits were identical. The conclusions deduced from this finding differ from those put forward by Lurie (*J. exp. Med.*, 1942, **75**, 247) and others, and the significance of this is discussed. *John M. Talbot*

946. **Evaluation of the Oxidation-reduction Dye Test for the Determination of Virulence of Mycobacteria *in vitro***
R. A. PATNODE, C. K. WRINKLE, and C. BEASLEY. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 599–603, April, 1954. 4 refs.

At the Communicable Disease Center, U.S. Public Health Service, Chamblee, Georgia, the oxidation–reduction dye test was applied to 1,033 cultures of acid-fast bacilli, including 760 of various species of *Mycobacterium*, the dyes employed being phenol indophenol, sodium benzenoneindophenol, sodium benzenoneindo-3′-chlorophenol, and sodium 2:6-dibromobenzenoneindophenol. Approximately 5 mg. of each of the cultures was added to each of the four tubes of dye, and after thorough shaking the tubes were examined at the end of 15 minutes for reduction. It is noted that viable organisms are necessary for a satisfactory test, so that old strains should be freshly subcultured.

In 327 strains there was 100% agreement between the results of the dye reaction and colony characteristics. In 706 strains there was 97% agreement between the dye reaction, colony characteristics, and virulence of the organism on injection into guinea-pigs; with the remaining cultures there were discrepancies of varying degree.

It is concluded, therefore, that the dye test in its present form cannot replace animal inoculation for the determination of the pathogenicity of mycobacteria, but that the test may still be of value in the laboratory diagnosis of tuberculosis. *R. B. Lucas*

947. **The Basis of Virulence in *Pasteurella pestis*: Attempts to Induce Mutation from Avirulence to Virulence**
T. W. BURROWS and G. A. BACON. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **35**, 129–133, April, 1954. 10 refs.

The hypothesis that virulent plague organisms have evolved from avirulent strains by mutation, or other change, and that existing avirulent laboratory strains represent reverse mutation, was tested by attempting to bring about artificial mutation of an avirulent strain " Tjiwidej " to the virulent form, using *x* rays as mutagenic agent and the mouse as a selective medium. From 237 trials one virulent strain was isolated, but cannot be proved beyond doubt to have arisen by mutation of the avirulent parent. Using nutritionally marked avirulent parents, no virulent organisms were recovered. The isolation of these biochemical mutants, with require-

ments for tryptophan, arginine, nicotinamide and adeninine respectively, is described.—[Authors' summary.]

948. **The Basis of Virulence in *Pasteurella pestis*: Comparative Behaviour of Virulent and Avirulent Strains *in vivo***

T. W. BURROWS and G. A. BACON. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **35**, 134–143, April, 1954. 5 figs., 21 refs.

The behaviour of virulent and avirulent strains of *Pasteurella pestis* in mice, especially the phagocytic response to the injected organisms, was investigated at the Microbiological Research Department, Porton, Wiltshire. Virulent and avirulent strains were grown for 18 hours at 37° C. and inoculated intraperitoneally into mice in which a peritoneal exudate rich in polymorphonuclear leucocytes had been produced by the injection of a 2% wheat-starch suspension. At intervals over a period of 5 hours pairs of mice from each series were killed, and from the peritoneal fluid smears were prepared and the number of ingested organisms was determined. It was found that at first both strains were readily ingested by the phagocytes, but that after about half an hour *in vivo* the virulent strains became progressively more able to resist phagocytosis, whereas the avirulent strains did not. For this resistance to develop, active metabolism by the organism appears to be essential; the resistance is apparently due in part to direct inhibitory action on the polymorphonuclear leucocytes and in part to a modification of the internal economy of the cell.

John M. Talbot

949. **Correlation of Biologic Properties of Strains of Mycobacterium with Their Infrared Spectrums. III. Differentiation of Bovine and Human Varieties of *M. Tuberculosis* by Means of Their Infrared Spectrums**

D. W. SMITH, W. K. HARRELL, and H. M. RANDALL. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 505–510, April, 1954. 4 figs., 4 refs.

950. **Further Notes on the Tissue Stages of *Plasmodium cynomolgi***

H. E. SHORTT, R. S. BRAY, and W. COOPER. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **48**, 122–131, March, 1954. 9 figs., 11 refs.

Up to the present, practically nothing has been known regarding the exo-erythrocytic development of the mammalian malaria parasite during the first 4 days after inoculation of the sporozoites into the host. This gap in our knowledge has led to speculations regarding the site in which the initial development takes place, some workers believing that the schizogonic cycle in the parenchymal cells of the liver was preceded by a cycle in cells of the reticulo-endothelial system (probably Kupffer cells), as in avian malaria. To settle these doubts, the authors undertook an experimental study of the earlier stages of pre-erythrocytic schizogony in *Plasmodium cynomolgi* to supplement the previous studies by the senior author and his associates of the development of this parasite in the liver cells from the 5th day onwards. As previously, *Macaca mulatta* monkeys were infected by multiple bites from *Anopheles maculipennis atroparvus* carrying the parasite. In addition, suspensions of the salivary glands or crushed bodies of infected mosquitoes were injected subcutaneously, intravenously, intraperitoneally, into the portal vein, or directly into the exposed liver in different monkeys, portions of the liver being removed by biopsy 2, 3, or 4 days later and examined in fixed and stained sections. In this way pre-erythrocytic parasites 2, 3, and 4 days old were identified, which are described in detail and beautifully illustrated in a set of coloured figures, showing beyond all doubt that all these forms are situated within the parenchymal cells of the liver. The 2-day forms are minute rounded bodies 2·3 to 2·45 μ in diameter with a single nucleus, in some cases showing signs of commencing division into two. On the 3rd day the parasite measures 4·5 to 5·9 μ and schizogony is well advanced, with at least 8 nuclei present. By the 4th day the schizont has grown to an average diameter of 10 μ and contains upwards of 20 nuclei.

The opportunity was also taken to study exo-erythrocytic development beyond the 12-day stage reported previously. On the 15th day a fully mature schizont was found, measuring 108 μ in diameter and estimated to contain some 60,000 merozoites, and a 17-day-old schizont was seen which was less advanced in development. These are regarded as "primary" schizonts, that is, belonging to the cycle initiated by the sporozoite after its invasion of the liver cell. Finally, in the liver of one of the experimental monkeys examined 105 days after infection were found 2 late schizonts of a type which is presumably responsible for relapses.

In none of the cases observed was there any evidence of a cellular reaction on the part of the host's tissues.

C. A. Hoare

951. **Factors Affecting the Efficiency of Combined Prophylactics. I. Effect of Diphtheria Toxoid and Pertussis Vaccine on Tetanus Toxoid**

L. LEVINE and J. L. STONE. *Journal of Immunology* [*J. Immunol.*] **72**, 258–262, April, 1954. 1 fig., 8 refs.

At the Massachusetts Department of Public Health, Boston, the effect on the potency of tetanus toxoid in mice of the addition of diphtheria toxoid or pertussis vaccine was investigated. The success of the immunization was assessed from the symptoms and from the survival time of the mice after a subsequent injection of tetanus toxin. It was found that the presence of the diphtheria toxoid had no significant effect on the immunity conferred against tetanus toxin. Pertussis vaccine in the prophylactic inoculum, however, materially increased the resistance of the animals to challenge with this toxin.

G. Payling Wright

952. **Cellular Vaccines and Toxoid in the Immunization of Animals against Diphtheria**

H. E. BOWEN, L. WYMAN, and J. A. MCCOMB. *American Journal of Hygiene* [*Amer. J. Hyg.*] **59**, 306–317, May, 1954. 1 fig., 15 refs.

Pharmacology

953. **Coronary Dilator Action. III. Effect of Several Antihistamine Compounds on Coronary Blood Flow in the Intact Dog**
M. M. WINBURY. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **110**, 300–303, March, 1954. 13 refs.

The coronary dilator action of six antihistamine compounds was studied in the dog, the rate of blood flow being measured continuously with a recording rotameter in circuit between one of the carotid arteries and the descending branch of the left coronary artery, and the effect of each drug being compared with that of 2-diethylaminoethyl di*cyclo*hexylcarbamate, the potency of which was regarded as 100. The relative potencies of the antihistamine compounds tested were: " RP-3015 " (10-(β-dimethylaminoethyl)-phenothiazine), 190; " diparcol " (diethazine), 51; " phenergan " (promethazine), 72; diphenhydramine, 59; " neo-antergan " (mepyramine), 30; " pyribenzamine " (tripelennamine), 6. It was of interest that coronary dilator activity appeared to be in rough inverse relation to antihistamine potency. Coronary dilatation with these compounds was not accompanied by any marked change in blood pressure, heart rate, stroke volume, or cardiac output. *R. Wien*

954. **A Comparative Study of the Action of Octaverine, Perparine and Papaverine on the Circulatory and Respiratory Systems**
A. A. GOLDBERG and M. SHAPERO. *Journal of Pharmacy and Pharmacology* [*J. Pharm. Pharmacol.*] **6**, 236–245, April, 1954. 2 figs., 28 refs.

Octaverine and perparine have been reported to be less toxic and to have greater spasmolytic activity than papaverine, of which they are synthetic analogues. In the present paper a study of their effects on the circulatory and respiratory systems is described. In heparinized rabbits anaesthetized with urethane the intravenous injection of 1 mg. of octaverine per kg. body weight caused an average fall in blood pressure of 30% (from 85 to 60 mm. Hg) lasting for 15 seconds, the pressure then rising steadily to reach its original level after 15 minutes; there was a slight increase in the depth but no change in the rate of respiration. A dose of 2 mg. per kg. caused a similar but more prolonged fall in the blood pressure, while both depth and rate of respiration were increased for 15 minutes. A dose of 4 mg. per kg. caused a 40% fall in blood pressure, the normal level being regained after one hour; respiration was increased in rate and depth, returning to normal after one hour. Perparine in a dose of 1 mg. per kg. caused a smaller and more transient fall in blood pressure than the same dose of octaverine, with an increase in depth of respiration. In a dose of 2 mg. per kg. it caused a fall in blood pressure as great as with the same dose of octaverine, although the effect only lasted for one minute, together with slowing of the heart and an increase in the amplitude of the beat; again the depth but not the rate of respiration was increased. A dose of 4 mg. of perparine per kg. caused a greater fall in blood pressure (50%) than the same dose of octaverine, but the effect lasted for only 4 minutes; both depth and rate of respiration were increased by this dose. Comparable doses of papaverine caused biphasic responses in the blood pressure, the fall in each case being followed by a rise. Both phases were transient, and the hypotensive effect was less than those of the other drugs.

Both octaverine and perparine were shown to be more effective than papaverine in antagonizing the rise in blood pressure caused by the intravenous injection of adrenaline in the rabbit, while the toxicity of intraperitoneal injections of adrenaline in mice was reduced by octaverine and by perparine, but not by papaverine. [These tests would have been more satisfactory if larger groups of animals had been used.]

In the isolated perfused rabbit heart octaverine was more effective and perparine less effective than papaverine in producing coronary dilatation. All the compounds decreased the amplitude of beat of the isolated heart, and in this respect papaverine was the most potent. *P. A. Nasmyth*

955. **The Pharmacological Actions of Andromedotoxin, an Active Principle from *Rhododendron maximum***
N. C. MORAN, P. E. DRESEL, M. E. PERKINS, and A. P. RICHARDSON. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **110**, 415–432, April, 1954. 10 figs., 31 refs.

Andromedotoxin, a nitrogen-free, neutral, crystalline substance isolated from the leaves of *Rhododendron maximum* has been studied. The rapid intravenous injection of andromedotoxin produces bradycardia, hypotension, and respiratory depression. Atropine prevents the bradycardia and diminishes the hypotensive component. Vagotomy abolishes the entire response. Three manometer technique studies demonstrate a reflex vasodilatation, as well as bradycardia, as contributing to the hypotensive effect. The minimal effective dose in eliciting this reflex is 2 to 3 μg. per kg.

A distinct hypotensive action in vagotomized animals occurs in a dose range of 2 to 20 μg. per kg., the magnitude of the depressor effect being proportional to the dose. Associated with this response is a blockade of the carotid sinus pressor reflex and the production of postural hypotension. The absence of a peripheral autonomic blocking action, the failure to obtain the response in the spinal cat, and the absence of direct vasodilatation on intra-arterial administration demonstrate a lack of peripheral action. Studies with the three manometer technique indicate a nerve mediated vasodilatation. It is believed that the action is a direct

depression of the vasomotor center or a stimulation of receptors in the head and neck with a reflex vasodilatation.

Electrocardiographic changes such as ventricular extrasystoles, A–V nodal and ventricular tachycardia, conduction impairment, and ventricular fibrillation occur with doses of 35 μg. per kg. and greater.

Andromedotoxin in doses of 40 μg. per kg. and greater causes a rise in blood pressure due largely to the release of epinephrine from the adrenal medulla, as shown by the absence of the greater part of the effect after adrenergic blocking doses of phentolamine and after adrenalectomy. Because of a transient venous pressure lowering effect, the possibility exists of a positive inotropic action on the heart as a contributory factor in this pressor effect.

A veratrine-like action on the isolated frog sartorius muscle appears in concentrations of 1:250,000, along with a progressive decrease in the twitch height. Unlike veratridine there is no significant initial increase in twitch height, only a delayed relaxation. Andromedotoxin also antagonizes the action of veratridine.

Emesis occurs in unanesthetized dogs upon parenteral administration of andromedotoxin in doses of 7 μg. per kg. and greater. Respiratory stimulation or depression occur in vagotomized dogs with doses of 20 μg. per kg. and greater. The mechanisms of these actions are unknown. Stimulation of the central nervous system followed by depression occurs with high doses. The actions of andromedotoxin are of short duration, lasting less than one hour even with toxic doses.

The close similarity in actions of andromedotoxin to the veratrum alkaloids has been discussed.—[Authors' summary.]

956. **Heparin and Ethyl Biscoumacetate in Prevention of Experimental Venous Thrombosis**

P. JEWELL, T. PILKINGTON, and B. ROBINSON. *British Medical Journal* [*Brit. med. J.*] **1**, 1013–1016, May 1, 1954. 7 figs., 9 refs.

The efficacy of heparin was compared with that of ethyl biscoumacetate in the prevention of thrombosis following experimentally induced phlebitis in rabbits. The sclerosing agent (0·1 ml. of monoethanolamine oleate) was injected into one of the marginal ear veins in the direction of the blood flow and held in a 4-cm. length of vein for 5 minutes. In this way, extensive thrombosis was produced. One group of 31 rabbits received ethyl biscoumacetate by mouth in 10- to 40-mg. doses twice daily for 3 days before the injection of the sclerosing agent. Administration of the anticoagulant drug was continued for another 5 days, the animals then being killed. Only 4 rabbits in this group showed extensive thrombosis. A second group of 34 rabbits received heparin as follows: an intravenous injection of 500 to 1,000 units every 6 hours (11 animals); intramuscular injection of 1,000 to 1,500 units every 6 hours (10 animals); intramuscular injection of 500 to 1,000 units every 4 hours (13 animals). Extensive thrombosis was found in 25 of the 34 veins tested, all three methods of heparin administration being equally unsuccessful in preventing thrombosis. It is considered that since the dosage of ethyl biscoumacetate was only slightly (two to three times) greater than that given to human beings, this difference between the efficacy of the two drugs is important.

[The authors' findings call for critical assessment of the value of these two drugs in the prevention of thrombosis in man.] *G. B. West*

957. **Comparative Effects of Newer Anticholinergic Agents on Human Gastric Secretion**

J. A. MCGOWAN and M. STANLEY. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **43**, 359–366, March, 1954. 10 refs.

At the New England Center Hospital, Boston, the effect on gastric secretion of atropine and 10 recent synthetic anticholinergic drugs (quaternary amines, six of which are identified only by their laboratory number) was observed after their administration to 109 patients, 25 other patients not receiving the drugs serving as controls. Nearly half of each group had active or healed peptic ulcer. Results were based on examination of the gastric contents after test meals given before and after the administration of the drug or, in cases of hypersecretion, on basal secretion values without meals.

From their findings the authors conclude that the drugs could be divided roughly into four groups in descending order of potency, the doses in brackets being those which diminished secretion by at least 20%: (1) atropine (1·3 mg.); (2) "antrenyl" and "Ro2-3773" (10 to 35 mg.); (3) "probanthine" (propantheline) (30 to 60 mg.), 2963 (75 to 125 mg.), "banthine" (methantheline), and 3199 (100 to 150 mg.); (4) 2998, 3505, 2806, and "prantal" (400 to 700 mg.). There was some dryness of the mouth in all cases, and it was noted that achlorhydria was attained more easily by parenteral than by oral administration. *V. J. Woolley*

958. **The Hematologic Response to Adrenaline**

V. W. GROISSER and W. RUBERMAN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **43**, 386–394, March, 1954. 2 figs., 24 refs.

The haematological response to injection of adrenaline in 26 patients with various disorders of the blood and in 9 patients suffering from other disease conditions but in whom the blood picture was normal is described. An intramuscular injection of 0·5 to 1 ml. of 0·1% adrenaline was given to all the patients, the blood count being determined before and at periods of 5 minutes to 4 hours after the injection. In all the cases the injection was followed by a leucocytosis, but no change was observed in the haemoglobin value or in the platelet count. The same response was obtained in patients subjected to splenectomy. The only condition in which the differential count was modified by the injection was aplastic anaemia, a decrease in the neutrophil and an increase in the lymphocyte counts being noted. It is suggested that the leucocytosis is due to an increased velocity of blood flow which brings more cells into circulation, and is not related to the spleen.

V. J. Woolley

959. **The Effect of a Dibenzazepine Derivative (Ilidar) on Renal Function**
C. A. HANDLEY and J. H. MOYER. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **110**, 277–281, March, 1954. 10 refs.

Renal plasma flow is increased in both man and unanaesthetized animals by " apresoline " (hydrallazine), a sympathetic depressant with a central as well as an anti-adrenaline action, whereas in anaesthetized animals apresoline depresses renal function. On the other hand such adrenergic-blocking drugs as " dibenamine " and " regitine " have little effect on renal function.

The effect on the kidneys of a hypotensive agent, " ilidar " (6-allyl-6:7-dihydro-5-dibenzazepine hydrochloride), was studied at Baylor University College of Medicine, Houston, Texas. It was found to reduce the blood pressure in anaesthetized dogs without depressing the glomerular filtration rate, renal plasma flow, or the maximum rate of tubular transport of glucose. Ilidar reduces blood pressure by a direct vasodilator action on the vessels as well as by adrenergic blockade, and in this way resembles " priscol " (tolazoline) which, however, depresses renal function in anaesthetized animals.

R. Wien

960. **The Influence of Plasma Electrolyte Concentration on Mercurial Diuresis in the Dog**
A. FARAH and F. KODA. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **110**, 361–368, March, 1954. 5 figs., 16 refs.

961. **A Clinical and Experimental Study of the Anti-rheumatic Activity of Amidopyrine Gentisate.** (Ricerche cliniche e sperimentali sull'attività antireumatica del gentisato di amido-pirina)
S. MAINOLI and O. PICCINELLI. *Minerva medica* [*Minerva med. (Torino)*] **1**, 787–791, March 21, 1954. 1 fig., 37 refs.

Amidopyrine gentisate (associated with amidopyrine and a synthetic antihistamine drug in a commercial preparation, " pirisal ") was given experimentally at the Institute of Clinical Medicine and Therapeutics of the University of Pavia to 15 normal subjects, 5 patients with acute articular rheumatism, 10 with rheumatoid arthritis, 7 with chronic rheumatism following acute arthritis, 10 with lumbar osteoarthritis, 8 with " rheumatic myalgia ", and 3 with humero-scapular periarthritis. It was given by mouth in doses containing 2·375 g. of amidopyrine gentisate and 0·375 g. of amidopyrine or by intramuscular injection in doses containing 0·375 g. of each, and 2, 4, and 6 hours after its administration an eosinophil count was carried out on the peripheral blood, together with estimation of the blood gentisate level. Apart from minor side-effects such as giddiness, the drug was well tolerated.

In all cases there was a reduction in the eosinophil count resembling that seen after administration of ACTH. In 10 patients the effect was compared with that of sodium gentisate, which caused an average reduction in eosinophil count of 13·4% compared with 38% when amidopyrine gentisate was given. Amidopyrine thus appeared to be the more active component part of the preparation. When the drug was given in the above dosage daily there was a definite reduction of pain in 90% of the patients with chronic rheumatism, within 1 or 2 days of starting treatment in cases of " rheumatic myalgia ", and in 10 to 12 days in cases of chronic polyarthritis. Acute rheumatism was less amenable, but even in these cases there was diminution of pain, temperature, and articular swelling after 4 or 5 days. The improvement in function was less obvious. In all cases in which the clinical response was satisfactory there was also some reduction in the erythrocyte sedimentation rate.

Cheapness and the possibility of prolonged administration without ill effect are claimed to be the main advantages of the drug, which was given in some cases after treatment had been started off with ACTH or cortisone. [It should be remembered, however, that prolonged administration of amidopyrine is not without danger of agranulocytosis. There have been recent reports that good results may be obtained with buffered salicylates, the use of which would therefore be preferable.]

V. C. Medvei

962. **A Search for More Effective Muscle Relaxants among the Glycerol Ethers and Dioxolanes**
J. S. GOODSELL, J. E. P. TOMAN, G. M. EVERETT, and R. K. RICHARDS. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **110**, 251–259, March, 1954. 2 figs., 23 refs.

A total of 507 compounds with muscle relaxant properties of central origin, like those of mephenesin, were studied. The majority contained the glycerol skeleton as glycerol ethers, dioxolanes, or benzodioxanes, the remainder including compounds of widely varying structure, among which were mono- and di-alcohols, imidazoles, and sulphones. The drugs were given by mouth to mice in various doses, the degree, time of development, and duration of muscular relaxation, the nature of other neurological symptoms, and the effect on the pinna and corneal reflexes being observed. The median paralytic dose (PD_{50}) of each compound was calculated as a measure of its potency. The glycerol ethers and dioxolanes provided the most consistent series of active compounds, and attention was focused on 44 of the former and 42 of the latter.

It was found that these centrally acting muscle relaxants abolished the pinna reflex before the corneal reflex, in contrast to many other types of central depressant, while the smooth onset and greater degree of the relaxation produced were other features which distinguished the glycerol ethers from hypnotics. In general, the duration of action decreased and potency increased with increasing molecular weight, potency reaching an optimum with a total of 10 to 12 carbon atoms in the molecule. The properties of one of the compounds tested—α-ethyl-γ-*iso*propylglycerol ether (" troxanol ")—are described in particular as representing a compromise between these two opposing trends. It is considerably less potent than mephenesin, but has a longer duration of action, and the combination of these two drugs is suggested for clinical use.

R. Wien

Chemotherapy

963. **Concentration of Antibiotics in the Brain**
W. E. WELLMAN, H. W. DODGE, F. R. HEILMAN, and M. C. PETERSEN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **43**, 275–279, Feb., 1954. 7 refs.

After the administration, usually for 24 hours preoperatively, of one of the six antibiotics, procaine penicillin, dihydrostreptomycin, erythromycin, aureomycin, " terramycin " (oxytetracycline), and " neo-penil " (the diethylaminoethylester hydriodide salt of benzylpenicillin) to 27 psychiatric patients in groups of 4, 5, or 6 undergoing prefrontal lobotomy at Rochester (Minnesota) State Hospital, the presence of the various antibiotics was determined in samples of blood, cisternal fluid, cerebrospinal fluid from the lumbar area, and brain tissue removed at the time of operation.

It was found that only neo-penil, aureomycin, and oxytetracycline were present in significant amounts in brain tissue. Dihydrostreptomycin was not found in brain tissue, but significant amounts were present in the serum and cerebrospinal fluid, while procaine penicillin and erythromycin were absent from both brain tissue and cerebrospinal fluid. It was noted that aureomycin, which is known to cross the blood–brain barrier, was in no case found in the cerebrospinal fluid. It is considered that these findings may be of significance in the choice of an antibiotic for the treatment of infections of the central nervous system. *R. Wien*

964. **Penethamate (Neo-penil): its Diffusion into the Cerebrospinal Fluid**
J. GYLFE, G. M. BAYNE, and W. P. BOGER. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 133–137, Feb., 1954. 1 fig., 17 refs.

The concentration in the blood and cerebrospinal fluid (C.S.F.) of penethamate (the diethylaminoethylester hydriodide of benzylpenicillin) was compared with that of procaine penicillin in 104 patients at Norristown State Hospital, Pennsylvania. At this hospital examination of the C.S.F. is a routine diagnostic procedure, so that for the period of this investigation alternate patients on admission were first given an intramuscular injection of 300,000 units of penethamate or procaine penicillin. In 18 of the 104 cases C.S.F. had to be withdrawn a second time, and these patients served as their own controls (making a total of 122 estimations in the series). The results were plotted on scattergrams. The penicillin in the plasma and C.S.F. was assayed by means of a modification of the *Sarcina lutea* cup-plate method.

The penicillinaemia resulting from the intramuscular injection of procaine penicillin was comparable with that following injection of penethamate. In none of the 54 instances in which procaine penicillin was given was there a detectable amount of the antibiotic in the C.S.F., whereas in the 68 in which penethamate was given there were average concentrations of 0·05, 0·07, 0·13, 0·06, 0·05, and 0·05 unit per ml. at 30 minutes, 1 hour, and 2, 3, 4, and 6 hours respectively. It is pointed out that these average figures mask the fact that in 19 of these 68 instances the C.S.F. did not contain any detectable amount of penicillin.

In view of recent reports of the toxicity of penethamate, the authors question its implied therapeutic value in the treatment of infections of the central nervous system. They suggest that for the present the safest method of achieving a high concentration of penicillin in the C.S.F. is by intravenous administration of water-soluble benzylpenicillin in a dosage of 6 to 12 mega units.
Norval Taylor

965. **Neo-penil: a Comparative Study of Blood, Urine and Lung Levels**
F. E. MURPHY, M. P. BRIGNOLA, and A. BONDI. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 398–402, April, 1954. 7 refs.

In an investigation carried out at the Hahnemann Medical College and Hospital, Philadelphia, the concentrations of penicillin in the blood and in the lungs after the administration of " neo-penil " (penethamate) in various doses were compared with those obtained with procaine penicillin and aqueous benzylpenicillin. It was found that neo-penil had a repository action similar to that of procaine penicillin, but the plasma level was somewhat lower. The concentration of penicillin in the lung tissue was invariably higher in patients receiving neo-penil than in those receiving the other two preparations. The amount of penicillin recovered from the urine varied from 44 to 51% of the total dose of procaine penicillin administered, whereas with neo-penil the amount excreted varied from 21 to 29% of the total dose.
A. W. H. Foxell

966. **Comparison of Sodium and Procaine Penicillin in Treatment of Experimental Staphylococcal Infection in Mice**
F. R. SELBIE. *British Medical Journal* [*Brit. med. J.*] **1**, 1350–1353, June 12, 1954. 3 figs., 7 refs.

In a study of the comparative effects of aqueous penicillin and depot penicillin carried out at the Bland-Sutton Institute of Pathology, Middlesex Hospital, London, four groups of 6 mice each were inoculated intramuscularly with an 18-hour culture of one of two strains of *Staphylococcus pyogenes*. The first group remained untreated and acted as a control, while the other three groups were treated respectively with an aqueous solution of the sodium salt of benzylpenicillin, a suspension of procaine penicillin in arachis oil containing 2% of aluminium stearate, and an aqueous suspension of procaine penicillin, the dose of each preparation containing 30,000 units of penicillin per 0·1 ml. The antibiotics were injected as far from the site of inoculation as possible.

All three preparations significantly reduced the size of the swelling at the site of infection, but none was demon-

strably better than either of the others. Determination of the concentration of penicillin in the animals' blood made at intervals after injection showed that during the first 10 minutes the serum concentration of sodium penicillin was five times greater than the highest level attained at any time by either of the other preparations, but from 30 minutes onwards it showed the lowest concentration. It was also noted that absorption of the aqueous solution was more rapid than that of the oily suspension of procaine penicillin, and that penicillin was detectable in the blood at least 4 days after the injection of the aqueous suspension as against 7 days with the oily preparation.

The author concludes that the curative effects of penicillin depend not so much on the aggregate time that an effective level of penicillin is maintained in the blood as on other factors, of which the most important is the cooperation of the defence mechanisms of the host. The application of these findings to the treatment of human infections is discussed at some length. It is concluded that it has not yet been proved in practice whether the prolonged penicillinaemia provided by procaine penicillin is more efficacious than the short-lasting but initially higher blood levels provided by sodium penicillin in the treatment of most infections amenable to penicillin therapy. *A. W. H. Foxell*

967. **Relation between Antibacterial Action of Penicillin and Mouse Host Defenses in Systemic Pneumococcus Infection**

D. W. Esplin and S. Marcus. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 423–432, April, 1954. 3 figs., 16 refs.

At the University of Utah College of Medicine the authors have carried out a series of experiments designed to assess the relative roles of penicillin and host defence mechanisms in pneumococcal infection induced in mice by the intraperitoneal injection of Type-III pneumococci. From their findings they conclude that leucocytes play a major local role in the host defence mechanism of the mouse. It was also demonstrated that adrenalectomized mice showed decreased resistance to infection, and that the administration of cortisone, but not that of adrenocortical extract, was capable of restoring to normal the resistance of the animals to intraperitoneal pneumococcal infection. *D. Geraint James*

968. **The Action of a New Antibiotic, Trichomycin, upon *Trichomonas vaginalis*, *Candida albicans* and Anaerobic Bacteria**

M. Magara, E. Yokouti, T. Senda, and E. Amino. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 433–438, April, 1954. 1 fig., 7 refs.

In this report from Nippon Medical College, Tokyo, the authors describe the results of a laboratory and clinical study of the new antibiotic, trichomycin, produced by *Streptomyces hachijoensis* and previously described by Hosoya *et al.* (*Jap. J. exp. Med.*, 1952, **22**, 505). It was effective in concentrations of 0·01 mg. per ml. against *Trichomonas vaginalis*, and 0·0005 mg. of the antibiotic inhibited the growth of 3 strains of *Candida albicans* in 48 hours. It was also effective in inhibiting the growth of a small group of anaerobic bacteria, including a strain of *Clostridium perfringens*.

In the clinical tests the insertion of vaginal tablets containing 50 mg. of trichomycin daily for 2 weeks in the treatment of patients with *Trichomonas* infection resulted in negative smears being obtained for 2 to 4 months, no toxic effects being observed. Similar treatment for 7 doses caused amelioration of symptoms and negative smears in patients with vaginal moniliasis. Trichomycin had effect on aerobic bacteria such as *Staphylococcus* and *Streptococcus haemolyticus*.

D. Geraint James

969. **Experimental Study on the Absorption of Oxytetracycline by the Stomach and the Small Intestine and its Excretion in the Bile**

E. Danopoulos, B. Angelopoulos, C. Zioudrou, and P. Amira. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 451–454, April, 1954. 6 figs., 3 refs.

It is well known that oxytetracycline when given by mouth is well absorbed by the gastrointestinal tract. Experiments were carried out at the University of Athens to determine the rates of absorption by the stomach and by the small intestine separately, and also the amount of oxytetracycline excreted in the bile. It was found that when dogs were given oxytetracycline by mouth the greater part of the amount administered was absorbed by the stomach, a small part being retained by the liver to be excreted in the bile. In dogs with a biliary fistula the antibiotic was excreted in the bile in a concentration which was two to three times higher than the concentration in the blood. The maximum level in the bile occurred 3 to 6 hours after the antibiotic had been given. Clinical observations in one patient with postoperative biliary fistula confirmed these findings. The authors state that the antibiotic is concentrated in the liver, not the gall-bladder. *A. W. H. Foxell*

970. **Stool Concentrations and Absorption of Chloramphenicol and its Palmitate in Babies**

A. L. Spiers. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **9**, 59–61, March, 1954. 8 refs.

At Stobhill General Hospital, Glasgow, infants under the age of 15 months were given crystalline chloramphenicol or chloramphenicol palmitate, and the concentrations of the antibiotic in venous blood, stools, and urine were determined. Chloramphenicol was assayed biologically against the El Tor vibrio by serial dilution of inactivated and filtered preparations of stool and urine.

It was found that crystalline chloramphenicol was effectively absorbed, the levels in the serum and urine being high; the concentration in the stool was always low. The palmitate was poorly absorbed, the concentration in the stool being high though variable. The palmitate is therefore recommended for conditions in which there are pathogens in the lumen of the bowel, but not for infections of the tissues or the urinary tract.

L. G. Goodwin

Infectious Diseases

971. **The Infrequent Incidence of Non-paralytic Poliomyelitis**
E. B. SHAW and M. LEVIN. *Journal of Pediatrics* [*J. Pediat.*] **44**, 237–243, March, 1954. 2 refs.

The authors state their conviction that in nearly every case in which the diagnosis of poliomyelitis can be established on clinical grounds, muscular weakness can be objectively demonstrated at one time or another to a greater or lesser degree. In support of this thesis they examined the course of 798 cases of poliomyelitis among patients admitted to the Children's Hospital, San Francisco, over a period of 3 years from 1950 to 1953. Of these only 31 (3·9%) ran a non-paralytic course, whereas the incidence of such cases in those notified to the California State Department of Health over the 5-year period 1948–53 was 31·2%. Of the 798 cases in their series, 281 were admitted in the pre-paralytic stage, and of these the 31 that finally turned out to be non-paralytic constituted 11%; the other pre-paralytic cases were shown ultimately by careful examination and follow-up to have developed some muscle weakness.

These results being considerably at variance with commonly expressed opinion, the authors describe in some detail the methods they use to detect even small degrees of weakness. They state that failure sometimes results from an inadequate period of observation without opportunity for follow-up. In some cases the weakness cannot be detected when the patient is recumbent in bed and is to be found only after he gets up. Mild degrees of weakness which are overlooked may lead to late disability and deformity which are completely preventable.

In the authors' opinion the number of non-paralytic cases in their series was probably even less than the figure stated because, almost without exception, cases so classified were amongst those in which the initial symptomatology was mild and equivocal. They assert that in many cases the diagnosis of non-paralytic poliomyelitis cannot be proved. *J. V. Armstrong*

972. **Changes in the Cerebrospinal Fluid in Poliomyelitis.** (Изменения спинномозговой жидкости при полиомиэлите)
V. V. KARTASHEVA. *Журнал невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **54**, 250–253, March, 1954. 3 figs., 7 refs.

In poliomyelitis, while the interrelation between the number of cells and quantity of albumin in the cerebrospinal fluid (C.S.F.) during the first days and later is important, it is equally important to note the intensity of the globulin reaction and to determine the albumin–globulin ratio. The increase in albumin content in poliomyelitis is generally not significant and the albumin component remains normal or is decreased. In the meningeal form of poliomyelitis the decreases in the quantity of albumin and the number of cells in the C.S.F. run parallel, whereas in other forms of poliomyelitis the cellular count decreases but there is a simultaneous increase in the albumin content. As this, however, may appear only in the later stages several investigations of the C.S.F. should be carried out. The glucose content is important in the differential diagnosis, but its increase has no prognostic value.

In differentiating between the meningeal forms of poliomyelitis and lymphocytic choriomeningitis it is important and helpful not only to consider the intensity of the globulin reaction and the increase in the albumin–globulin ratio, which is so characteristic of the latter, but also to note the changes in the cell count, which in poliomyelitis becomes normal very quickly, but in lymphocytic choriomeningitis remains high for a long time. *H. W. Swann*

973. **Laboratory Investigations during Treatment of Patients with Poliomyelitis and Respiratory Paralysis**
P. ASTRUP, H. GØTZCHE, and F. NEUKIRCH. *British Medical Journal* [*Brit. med. J.*] **1**, 780–786, April 3, 1954. 11 figs., 4 refs.

This paper summarizes the experience gained by the authors from biochemical investigations carried out in cases of poliomyelitis with respiratory paralysis at the Blegdam Hospital, Copenhagen, during the epidemic of 1952. In most cases artificial respiration was applied by a manual intermittent positive-pressure technique through a tracheotomy tube (Lassen, *Lancet*, 1953, **1**, 37; *Abstracts of World Medicine*, 1953, **13**, 457), though a few patients were treated in cuirass and tank respirators. Measurement of the *p*H and carbon dioxide tension of the blood were found to provide valuable guides in assessing the effectiveness of pulmonary ventilation. Estimation of the alveolar CO_2 tension would also have been of great value, but difficulty was encountered in devising a simple and accurate method for use with the apparatus employed for artificial respiration. The degree of oxygen saturation of arterial blood proved of little value as an indication of the need for more or less ventilation, low values being found in some cases in association with over-elimination of CO_2 owing to uneven ventilation or the presence of areas of pulmonary collapse.

All patients treated in cuirass respirators developed a low blood *p*H and a marked rise in arterial CO_2 tension, indicating inadequate ventilation. Oxygen administration overcame the anoxaemia, but the danger of death from acidosis remained in such cases. The number of patients treated in tank respirators was too small for the collection of useful information. With the manual positive-pressure technique there was a natural tendency towards over-ventilation, and the authors point out that this method may also be a source of danger to the circulation, since a proportion of the pressure applied during the inspiratory phase will be transmitted to the media-

stinum and great veins, and the decrease thus caused in the venous return to the heart may be sufficient to lead to a fall in cardiac output and a state of shock. They conclude that " the least harmful method of positive-pressure ventilation with regard to the circulation should have (*a*) a low frequency, (*b*) a short inspiratory positive-pressure phase, and (*c*) a long expiratory phase with a rapid fall of pressure to zero, where it remains until the next inflation ". [These recommendations are timely and should be borne in mind by makers of mechanical positive-pressure apparatus before new machines are placed on the market.]

Numerous other observations of importance are reported, such as an increase in potassium excretion (due to the destruction of paralysed muscle), evidence of disturbance of liver function owing to changes in the circulation, and an increased tendency to bleed owing to decreased capillary resistance (probably the result of anoxia). The last two observations will be the subject of further papers by other authors.

[This article is the product of thorough and painstaking work. It should be read and studied by all those who wish to obtain the best physiological results with every type of apparatus for artificial respiration.]

L. J. M. Laurent

974. **Corticotropin (ACTH) in Severe Tetanus**

R. A. Lewis, R. S. Satoskar, G. G. Joag, B. T. Dave, and J. C. Patel. *Indian Journal of Medical Sciences* [*Indian J. med. Sci.*] **8**, 1–14, Jan., 1954. 11 figs., 18 refs.

Because of previous experience of the beneficial effect of adrenal hormone therapy in convulsions induced in animals by exposure to reduced oxygen tension the authors were encouraged to study its effect on tetanus. From cases of tetanus admitted to the King Edward Memorial Hospital, Bombay, only the most severe were selected for study, at least four of the following being required to be present: (A) trismus; (B) convulsions while under observation; (C) an incubation period of 7 days or less; (D) an onset period of 48 hours or less; (E) a rectal temperature of 100° F. (37·8° C.) or more within 24 hours of admission or within 48 hours of the onset of convulsions. Treatment with intravenous ACTH (corticotrophin) was given in alternate cases satisfying these criteria, each patient receiving 20 to 25 mg. of ACTH dissolved in 2 litres of 5% glucose solution 8- or 10-hourly at first, the last 5 patients out of 10 treated receiving the same dose 2-hourly at the beginning of treatment. The duration of treatment varied from 4 to 8 days and the total dose of ACTH from 80 to 160 mg. The 10 control subjects were given intravenous injections of 5% glucose, and all the patients received routine treatment, such as tetanus antitoxin, penicillin, and wound toilet.

The most striking effect of ACTH was on the fever, the temperature in treated cases being sometimes normal by the third day, especially when more frequent doses were given at the beginning. The respiration and pulse rates were also reduced. The part played by ACTH in the relief of trismus and the reduction of convulsions was more difficult to evaluate, but some relief was usually obtained after the second day of treatment and in several cases there was a return or an aggravation of the spasms when the dose of ACTH was reduced or omitted. An attempt was made to follow the course of the eosinophil count, but this was found to be depressed by the tetanus toxin, reaching zero by the second day in all fatal cases but one, and, in the survivors, tending to rise towards normal during the phase of recovery. It was noted, however, that even when the eosinophil count was zero a beneficial clinical effect was still obtained by giving ACTH, suggesting that although in tetanus there is a great outpouring of adrenal hormones, even more can be elicited by treatment with ACTH. Toxic effects from the ACTH were not marked, as the drug was not administered over long periods.

Among the 10 patients treated with ACTH there were 4 deaths, and among the 10 control subjects 7. Although the series is too small to have statistical value, it is considered significant that none of the patients receiving ACTH succumbed after completing 48 hours of treatment.

J. V. Armstrong

975. **Muscular Relaxation in Tetanus with Special Reference to the Effect of Mephenesin**

R. S. Diaz-Rivera, F. Trilla, and E. R. Pons. *Annals of Internal Medicine* [*Ann. intern. Med.*] **40**, 563–580, March, 1954. 14 refs.

976. **Penicillin Treatment of Scarlet Fever.** [In English]

J. Ström. *Acta paediatrica* [*Acta paediat.* (*Uppsala*)] **43**, 32–37, Jan., 1954. 29 refs.

Since 1946 penicillin has been given in all cases of scarlet fever at the Stockholm Hospital for Contagious Diseases, and in this paper the results obtained in some 6,500 cases are reported. The antibiotic was given in varying dosages, by injection or by mouth, for not less than 6 days. There were 447 control cases [but it is not clear how these were chosen, and they were treated for the most part at a different time from the others]. The incidence of complications, especially of myocarditis, lymphadenitis, and otitis, was considerably higher in the controls than in the treated patients. There was little to choose between the two routes of administration as regards complications.

R. S. Illingworth

977. **Penicillin in the Prevention of Scarlet Fever.** [In English]

J. Ström. *Acta paediatrica* [*Acta paediat.* (*Uppsala*)] **43**, 38–42, Jan., 1954. 4 refs.

Penicillin was given by mouth or by injection to patients with scarlet fever at the Stockholm Hospital for Contagious Diseases, and the incidence of haemolytic streptococci in the throat in such patients was compared with that in untreated patients. It was found that haemolytic streptococci rapidly disappeared from the nose and throat of the treated patients, whereas a high proportion of the controls, even though they were isolated, were carriers of streptococci when they left hospital. Furthermore, as a result of penicillin therapy recurrences and secondary cases among the staff of the hospital were extremely rare.

R. S. Illingworth

Tuberculosis

DIAGNOSIS AND PROPHYLAXIS

978. **Comparison between the International Standard Tuberculins, PPD-S and Old Tuberculin**
F. B. SEIBERT and E. H. DUFOUR. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 585–594, April, 1954. 17 refs.

The Expert Committee on Biological Standardization of the World Health Organization has chosen the purified protein derivative as prepared by Seibert (P.P.D.-S.) for its international standard for human (P.P.D.) tuberculins. In this paper from the University of Pennsylvania some precise comparisons between this standard and the batch of old tuberculin which has served as the International Standard Old Tuberculin (O.T.) are recorded; the British P.P.D. made in the Weybridge Laboratories was also included in the investigation.

An intradermal injection of 0·1 ml. of the proper dilutions of each tuberculin was given into the volar surface of the forearm of patients attending a tuberculosis clinic. Reactions were measured after 48 hours by two observers who were unaware of the identity of the tuberculin injected at each site. When the dilution of O.T. was found at which the reaction in highly sensitive subjects was equivalent to that of a given weight of P.P.D.-S. it was noted that the dilutions at which the two tuberculins gave equivalent reactions in less sensitive patients were not in the same proportion. The converse held for dilutions found to be equivalent in less sensitive patients. These results suggest that there are different antigens (or different proportions of the same antigens) in the two types of tuberculin; evidence in support of this has been found in immuno-chemical studies of the tuberculins. *J. E. M. Whitehead*

979. **Comparison of Plasma Viscosity and Erythrocyte Sedimentation Rates in Pulmonary Tuberculosis**
L. BENSON and J. GODDARD. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 595–598, April, 1954. 2 figs., 1 ref.

In a study of the comparative value of the plasma viscosity and the erythrocyte sedimentation rate as indicators of the presence of organic disease, carried out at Vermont Sanatorium, Pittsford, Vermont, over 5,000 determinations of these two values were made over a period of 4 years on 420 patients with pulmonary tuberculosis. It was found that in 15% of patients with active disease the erythrocyte sedimentation rate was normal, but that the plasma viscosity value was normal in only 5%. Similarly, in patients with inactive lesions the sedimentation rate was consistently normal in only 80% of cases, while the plasma viscosity values were within normal limits in 98% of the same group.

There was no relation between plasma viscosity and the haematocrit value, nor was viscosity altered by anaemia or during menstruation. There was, however, a small rise (to 1·8) in viscosity during the last 3 months of pregnancy. No relation could be established between total protein level and plasma viscosity. The authors conclude that the value for plasma viscosity (which is normally 1·7 times that of distilled water at 20° C.) is a more sensitive indicator of the presence and degree of activity of pulmonary tuberculosis than the erythrocyte sedimentation rate. A simple apparatus for the determination of plasma viscosity is described. In this series the highest plasma viscosity value observed was 2·8 and the lowest 1·5. *R. B. Lucas*

980. **Lupus Vulgaris following B.C.G. Vaccination**
P. V. MARCUSSEN. *British Journal of Dermatology* [*Brit. J. Derm.*] **66**, 121–128, April, 1954. 1 fig., 22 refs.

The literature before 1952 contained only 3 case reports of the development of lupus vulgaris at the site of B.C.G. inoculation; 3 further cases, seen at the Finsen Institute, Copenhagen, are described in the present paper and all 6 cases are discussed. In only one of the cases from the literature were bacilli of a strain indistinguishable from B.C.G. recovered from culture of a biopsy specimen, but the history and pathology in the other 2 cases suggested that in all probability they also were due to vaccination.

In the first case in the present series, that of a girl aged 17 who was tuberculin-negative and came from a non-tuberculous environment, a lesion which was histologically tuberculous developed from a papule at the inoculation site. The virulence of the strain isolated on subculture after 2 months' growth in Löwenstein's medium paralleled that of B.C.G. The reaction to subsequent tests with 1 in 100,000 tuberculin was positive. In the second case, that of a girl of 15 who had previously been inoculated three times without success, a fourth vaccination was followed by ulceration, fever (which soon subsided), and a slow-growing skin plaque with regional adenitis, which persisted. Culture of the pus from a fistula associated with the adenitis yielded organisms indistinguishable from B.C.G. In the third case, that of a youth aged 16 who was tuberculin-negative before vaccination but whose mother suffered from lupus, a lesion about 100 sq. cm. in area developed at the site of inoculation. Tubercle bacilli were cultured from this lesion, but their virulence was not determined. Both the second and third patients were sensitive to 1 in 10,000 tuberculin. In none of these 3 cases was there evidence of other tuberculous disease, and all responded to treatment.

The author, quoting Jensen and others, contends that the virulence of B.C.G. is only slightly lower than that of bacilli isolated from lupus tissue and, furthermore, that the infection of the skin and lymph nodes produced by

B.C.G. is in many cases clinically and pathologically indistinguishable from tuberculosis colliquativa, which often precedes lupus. For these reasons he advocates an observation period of not less than 5 years in all cases in which granulation tissue persists after vaccination. [These conclusions appear reasonable but, as the author himself points out, post-vaccinal lupus is so rare that no change in the general evaluation of B.C.G. vaccination is justified.] *R. J. Matthews*

981. **BCG-Vaccination Campaign in Aden Colony**
H. MØLLER, K. BERG, and H. CHRISTENSEN. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **10**, 113–125, 1954. 3 figs.

Under the auspices of the World Health Organization and the United Nations Children's Fund (UNICEF) a campaign of mass B.C.G. vaccination was carried out in the colony of Aden in the months of February to May, 1952, during which period 31,287 persons (about one-quarter of the population) whose ages ranged from 6 to 18 years were tuberculin tested with purified protein derivative (P.P.D.), a dose of 5 tuberculin units being injected intradermally. The reaction was observed after an interval of 3 or 4 days, an area of reactive induration of 5 mm. or more in diameter being regarded as positive.

Of the 22,110 persons completing the test, 14,345 (64%) showed a positive reaction. The frequency of positive tuberculin reactors rose from an average of about 33% at age 6 years to 65% at 14 years; the difference in the frequency of positive reactors as between boys and girls was small. Of the 7,785 persons who gave a negative reaction, 7,751 were vaccinated, 2,135 (27·5%) of these belonging to the age group 0 to 6, 4,795 (62%) to the age group 7 to 14, and 821 (10·5%) to the age group 15 years and over. The allergy induced by B.C.G. vaccination was similar in strength to that produced by natural infection. The skin reactions noted after vaccination ranged from indurated lesions to crusted lesions and scars, and in some 8% of the children there were still unhealed ulcers 9 to 11 weeks after vaccination.
Franz Heimann

982. **The Effect of Cortisone on BCG Infection in the Guinea Pig**
K. BIRKHAUG. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 511–519, April, 1954. 5 figs., 14 refs.

Administration of cortisone to guinea pigs inoculated with living or killed BCG vaccine produced a significant reduction in the inflammatory response to BCG and to tuberculin and restricted the intradermal spread of a vital dye.

The hemogram of BCG-sensitized animals treated with cortisone showed early eosinopenia, accelerated lymphopenia, and monocytosis (increased monocyte/lymphocyte ratio), but no sustained changes in the total erythrocytes and leukocytes, hemoglobin, or erythrocyte sedimentation rate. Necropsy material from BCG-sensitized animals treated with cortisone showed a significant reduction of hyperplasia in regional and distal lymph nodes and in the spleen, marked adrenal atrophy, but no sign of exacerbation of BCG lesions. Cortisone treatment during the active period of sensitization with BCG produced a significant increase in specific resistance against a challenge infection, which was most marked in animals sensitized with living BCG.

No other evidence was found that the administration of cortisone during and after the active phase of sensitization augmented the virulence of BCG.—[Author's summary.]

RESPIRATORY TUBERCULOSIS

983. **The Unhospitalized Tuberculous Patient**
A. B. ROBINS, H. ABELES, A. D. CHAVES, M. H. ARONSOHN, J. BREUER, D. WIDELOCK, and L. PEIZER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 26–36, Jan., 1954. 2 refs.

To determine the place of chemotherapy (with isoniazid) of the ambulatory patient in the control of pulmonary tuberculosis, 110 out of 9,000 such patients known to the New York Department of Health were selected for treatment with isoniazid in a dosage of 3 mg. per kg. body weight daily. Selection was dependent on repeated findings of tubercle bacilli in the sputum within the last 6 months, presence of fibro-caseous disease unsuitable for collapse or surgical therapy, and a cooperative attitude in the patient and his family. Of the original 110 patients, 22 did not complete the full course of 8 months' treatment, in most cases owing to death, hospitalization, or toxic reaction.

The maximum effect of the drug was reached in the first 3 months, most of the patients gaining weight and reporting reduction in the amount of sputum. There was marked radiological improvement in 47% of those completing 8 months' treatment, and the sputum became negative in 18%. The response was generally more favourable in those patients whose disease was of less than 5 years' duration. Radiological deterioration was observed in 11% and was associated with the presence in the sputum of tubercle bacilli which were resistant to isoniazid in concentrations of at least 1 μg. per ml., none of the strains originally isolated having been resistant to 0·1 μg. per ml.

The authors are of the opinion that the ambulatory treatment with isoniazid of suitable cases of pulmonary tuberculosis has a definite place in the fight against tuberculosis in view of the present universal shortage of hospital beds. *Franz Heimann*

984. **Combined Rest and Exercise in the Treatment of Minimal Tuberculosis. A Follow-up Study of One to Thirty Years**
E. N. PACKARD and P. F. FLYNN. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 50–57, Jan., 1954. 14 refs.

A series of 152 patients—82 males and 70 females—ranging in age from 17 to 46 years and suffering from early, uncomplicated pulmonary tuberculosis, were treated by combined rest and graduated exercise at the Trudeau Sanatorium, New York, during the period

1921–9 and have been followed up for 1 to 30 years after discharge. The patients' presenting symptoms varied widely, and included fatigue, loss of weight, cough, expectoration, haemoptysis, and pain in the chest. In 65 cases (43%) tubercle bacilli were found in the sputum. Previously the treatment of such forms of early tuberculosis had consisted in absolute rest, but in 1921 the authors introduced a modified scheme whereby, after an observation period of 2 to 3 weeks' complete rest, the patient was allowed a gradually increasing and strictly regulated amount of exercise. A review carried out in 1951–2 showed that 128 of the 152 were well when last heard of—40 of them 26 to 30 years, and 69 others 21 to 25 years, after discharge—3 were disabled by tuberculosis 26 to 30 years later, and 12 had died of tuberculosis and 9 from other causes. The authors suggest that these results compare favourably with those obtained with strict bed rest. *Franz Heimann*

985. **The Results of One Year's Treatment with Isoniazid in Relation to Bacterial Resistance.** (Ein Jahr Therapie mit Isoniacid. Bakteriologische Resistenz- und Therapie-Resultate)
G. MEISSNER and G. BERG. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **111**, 340–352, 1954. 12 figs., 17 refs.

From a study of the isoniazid sensitivity of tubercle bacilli isolated from cases of pulmonary tuberculosis before treatment with isoniazid and again 3 to 6 months afterwards, the authors have come to the conclusion that primary resistance to isoniazid seldom occurs and, when it does, is no contraindication to treatment with the drug. Among 1,717 strains isolated from 1,058 patients at the Borstel Institute for Tuberculosis Research, only one was resistant before treatment, while 2 others showed reduced sensitivity. Secondary resistance had developed in 13% of 883 sputum-positive cases after 4 weeks' treatment, rising to 65% at 3 months, to 78% at 6 months, and to 91% after 10 to 11 months' treatment. The development of bacillary resistance appears to occur more readily the greater the number of strains and cavities present. Of 523 patients who received no form of treatment other than isoniazid, the sputum had become negative in 46% after 3 months and in a further 20% after 6 months, but in all but 2% of the latter improvement had begun during the first 3 months. The authors therefore conclude that if treatment with isoniazid has no beneficial effect in the first 3 months, its continuation for a further period is unlikely to be successful. *Franz Heimann*

986. **The Treatment of Tuberculous Serofibrinous Pleurisy with ACTH.** (Le traitement des pleurésies séro-fibrineuses tuberculeuses par l'ACTH)
R. EVEN, C. SORS, Y. TROCME, and A. SARRAZIN. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **70**, 137–149, Feb. 12, 1954. 14 refs.

The authors report the treatment of 7 cases of tuberculous pleural effusion with ACTH (corticotrophin) combined with streptomycin and PAS. The ACTH was given intravenously dissolved in 500 ml. of PAS solution or glucose-saline over a period of 8½ hours each day. In the first cases 20 mg. of ACTH was given daily, but this was later reduced to 10 mg. daily. The intravenous route was chosen so that small doses of ACTH could be given, but the authors considered that it could also be given intramuscularly in doses of 75 to 100 mg. daily.

In 4 acute cases of pleural effusion the results were spectacular, the temperature falling almost immediately with absorption of the fluid so that after 15 days it had disappeared, leaving no *x*-ray evidence of residual pleural involvement. In 2 subacute cases, although there was absorption of the pleural fluid, this was not complete and left some pleural thickening. The erythrocyte sedimentation rate also remained raised. In one case in which fluid had appeared in an artificial pneumothorax this disappeared after 10 days, leaving no residual pleural thickening.

The authors discuss the role of ACTH in the treatment of tuberculous infections and suggest that in the special circumstances of pleural effusion the tubercle bacillus should be attacked with antibiotics and the non-specific reaction of inflammation with ACTH. *G. M. Little*

987. **Special Indications for Cortisone and ACTH in the Treatment of Pulmonary Tuberculosis.** (Y a-t-il des indications exceptionnelles de la cortisone et de l'ACTH dans le traitement de la tuberculose pulmonaire?)
H. P. KLOTZ, A. GUEZ, and B. MORIN. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **70**, 150–153, Feb. 12, 1954. 23 refs.

Two cases of pulmonary tuberculosis are described in which remarkable results were achieved, in one with ACTH and in the other with cortisone. Both the patients were North Africans whose general condition before treatment was very grave and had failed to respond to a prolonged course of chemotherapy. The first was a patient aged 40 with enlarged mediastinal glands which had ruptured into the trachea and had later produced an excavated focus at the left base. After one month's treatment with PAS, isoniazid, and streptomycin the condition was worse, but on starting treatment with ACTH in a dosage of 200 mg. daily the temperature immediately fell to normal and the patient began to put on weight. This treatment was continued for one month, and although the sputum was positive for the first time at the end of this period, the patient's general condition was markedly improved. The second patient had a tuberculous pleural effusion following an artificial pneumothorax and had made no response to large doses of PAS, streptomycin, and isoniazid given for 15 days. When cortisone in doses of 50 mg. daily was associated with the chemotherapy the temperature immediately fell, with improvement in the general state. Arguing from the work of Lurie on rabbits, the authors conclude that although cortisone favours the spread of tuberculosis in the body, it also raises the resistance of the host, and that there may be a place for this drug in the treatment of cases where resistance is low, as shown by the inability to respond to chemotherapy. *G. M. Little*

988. **Radio-iodine Measurements of Thyroid Function during and after P.A.S. Treatment of Tuberculosis**
J. A. BALINT, R. FRASER, and M. G. W. HANNO. *British Medical Journal* [*Brit. med. J.*] **1**, 1234–1237, May 29, 1954. 14 refs.

In this paper from the Postgraduate Medical School of London the authors report an investigation into the thyroid function of patients who had received prolonged treatment with PAS, the study being undertaken in view of reports of the development of hypothyroidism and goitre following the use of this drug. By measuring the thyroid activity by means of radioactive iodine (^{131}I) in patients during treatment with PAS, and again from 4 to 7 days after cessation of treatment, they sought to demonstrate that there was increased thyroid activity after withdrawal of the drug.

In all, 30 tuberculous patients were studied, most of whom had been receiving about 20 g. of PAS daily for 3 months or longer. Thyroid function was assessed by determining the urinary excretion of ^{131}I following a test dose of the isotope, the urine for estimation being collected over two periods of 24 and 48 hours, it being hoped by using the longer excretion period to nullify the effect of varying levels of PAS in the blood. The finding of a significant reduction in excretion of ^{131}I after withdrawal of PAS, reflecting increased thyroid uptake of ^{131}I, showed that within a few days of withdrawing the drug thyroid activity was increased above the level found during its administration, and above that of 30 normal control subjects. Of 11 patients who had received PAS for 6 months or more, 10 showed marked increase in ^{131}I uptake, and 4 had small goitres, suggesting that the longer the course of PAS the greater the thyroid depletion. There was, however, a noticeable individual variation in the antithyroid effect of the drug. In 2 of these patients the administration of iodide was followed by a rapid reduction in the size of the goitre and return to normal thyroid function.

In further experiments *in vitro*, based on the inhibition of iodination of protein, both PAS and isoniazid were shown to have weak antithyroid potency when compared with that of 2-thiouracil. This appeared to confirm the theory that PAS acts like other aminobenzene compounds by inhibiting iodination of the thyroid hormone.

J. N. Harris-Jones

989. **Results of Treatment of Ulcerocaseous Pulmonary Tuberculosis with a Combination of Streptomycin, Isoniazid, and *para*-Aminosalicylic Acid for at Least Six Months.** (Résultats du traitement de la tuberculose pulmonaire ulcéro-caséeuse par l'association streptomycine, isoniazide et acide para-amino-salicylique administrée pendant au moins six mois)
C. GERNEZ-RIEUX, M. GERVOIS, H. BEERENS, and P. FOURNIER. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] **18**, 1–25, 1954. 7 figs., 28 refs.

This is an account from Calmette Hospital and the Pasteur Institute, Lille, of the treatment of 75 cases of pulmonary tuberculosis for at least 6 months with streptomycin combined with isoniazid and PAS. There were 41 men and 34 women in the series, and their ages ranged from under 20 to over 60 years. Radiologically, the cases were divided into those with "slight" (22 cases), "moderate" (30 cases), and "extensive" lesions (23 cases). The dose of streptomycin was 1 g. every second day; that of PAS 15 g. each day, intravenously for the first 2 months and then by mouth; and that of isoniazid 5 mg. per kg. body weight each day. All cases were carefully followed up clinically, radiologically, and bacteriologically. The number of patients with normal temperature, increased weight, normal erythrocyte sedimentation rate, and absence of tubercle bacilli from the sputum at 2-monthly intervals showed a steady improvement. Radiologically, the greatest improvement was found in the group with slight lesions, while in 34·8% of the patients whose lesions were initially of the greatest severity no change was noted. Bacteriological findings were positive in 89% of cases before treatment, in 52% after 2 months, 32% after 4 months, and 20% after 6 months. Of 61 cases with positive cultures before treatment, in 55% the organisms were resistant to streptomycin after 2 months, 14·1% after 4 months, and 25% at the end of 6 months. The corresponding figures for resistance to PAS were 0, 4·7%, and 8·3%, and to isoniazid 2·75%, 9·4%, and 33·3%.

Of the original group, 26 remained under treatment in hospital for a further 7 to 12 months, and 22 were discharged from hospital and did not receive a standard course of treatment. At the end of 6 months, among those patients who remained in hospital there were 5 who had improved greatly with treatment, 13 with "substantial" improvement, and 5 in whom slight improvement had taken place. After further treatment 18 improved greatly and 4 made substantial progress. The 22 patients who left hospital were followed up for periods of 3 to 9 months. In 15 of these cases no further treatment was given, but the improvement was maintained.

[The differences in choice of cases and technique of treatment make it impossible for comparisons to be made with the Medical Research Council investigation.]

T. M. Pollock

990. **Viomycin Therapy in Human Tuberculosis**
H. G. SCHAFFELD, B. GARTHWAITE, and J. B. AMBERSON. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 520–542, April, 1954. 8 figs., 10 refs.

The results of administration of viomycin in 23 cases of tuberculosis, in 21 of which there was advanced pulmonary disease, are described. In 11 of the cases the tubercle bacilli were known to be resistant to streptomycin. Viomycin was given by intramuscular injection in a dosage of 50 to 60 mg. per kg. body weight daily; later this dosage was given twice a week. Improvement was "marked" in 8 cases, "moderate" in 5, and "slight" in 4; in 6 the disease condition was unchanged. There were varying degrees of improvement in extrapulmonary lesions, which occurred in 9 cases. In no case did viomycin aggravate the disease process.

Deafness was the most serious toxic manifestation, a high-frequency hearing loss being noted in 11 patients; in only 2 patients was there deafness to conversation. Hypokalaemia was found in 12 patients, being so severe

in 2 that potassium had to be given parenterally for 2 weeks. Albuminuria, which was transient, occurred in 14 cases. No skin changes were observed. The authors consider that viomycin is more effective than PAS, but probably less effective than streptomycin or isoniazid, and that it is indicated in cases in which there is resistance to the two last-named drugs. They were unable to study bacterial resistance in this small investigation, but suggest that a combination of viomycin and streptomycin or of viomycin and PAS may delay the emergence of resistant strains. Several full case histories are included. *Paul B. Woolley*

991. **The Use of Viomycin in Patients with Pulmonary Tuberculosis**

J. D. ADCOCK, W. N. DAVEY, R. R. HALEY, R. M. REES, and W. A. MEIER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 543–553, April, 1954. 2 figs., 13 refs.

An investigation was carried out at the University of Michigan Hospital, Ann Arbor, primarily to determine the toxic effects of viomycin in pulmonary tuberculosis. The drug was given to 12 patients with advanced pulmonary tuberculosis in a dosage of 40 to 60 mg. per kg. body weight a day for periods of 7 to 244 days. A skin rash developed in 4 patients, and in one an exfoliative dermatitis appeared on the 7th day. Albuminuria occurred in 8 of the patients, but was transient in 7; occasionally granular casts were present in the urine of these patients. The blood urea level was normal. There was some hearing loss in 3 out of 4 patients who had tinnitus, the deafness being sudden in onset in one. No evidence of hepatic damage was found and no significant change was observed in the serum electrolytes. Of the 7 patients with exudative disease improvement was marked in 2 and moderate in 5; there was improvement also in 2 patients with endobronchitis. The authors consider that viomycin is less effective than streptomycin, but that it can be given in cases of advanced disease which have become resistant to streptomycin. Care is required, however, in the administration of viomycin.

Paul B. Woolley

992. **The Treatment of Pulmonary Tuberculosis in Adults by Resection**

H. T. THOMPSON, T. SAVAGE, and T. H. L. ROSSER. *Thorax* [*Thorax*] **9**, 1–9, March, 1954. 7 figs., 8 refs.

This report from Sully Hospital, Glamorgan, on the surgical treatment of pulmonary tuberculosis is based on 266 consecutive resections performed on 259 patients. Resection is indicated, in the authors' opinion, in the presence of the following types of lesion: (1) the tuberculous cavity, (2) the solid tuberculous lesion, (3) tuberculous bronchiectasis, and (4) tuberculous bronchostenosis. Tuberculous empyema may complicate any of these lesions or they may represent failures of collapse therapy. Streptomycin resistance is regarded only as a relative contraindication to resection.

In addition to the usual investigations and general treatment, preparation for operation should include: (1) postural treatment in cases of cavitation to reduce or close the cavity; (2) chemotherapy with 1 g. of streptomycin and 20 g. of PAS daily for 7 to 10 days before operation (and continued after it); and (3) instruction in breathing exercises and coughing.

Some 2 weeks after pneumonectomy an 8-rib thoracoplasty is recommended in the belief that it will prevent late bronchopleural fistula and prevent mediastinal displacement and overdistension of the remaining lung. A limited apical thoracoplasty (3, 4, or 5 ribs) is advisable 3 to 6 weeks after lobectomy or multiple segmental resections, where palpable disease has been left in the remaining lung tissue, or where there is a persistent apical air pocket. Phrenic crush is the usual procedure after lower lobectomy.

In the series reported there were 5 deaths within 3 months of operation, giving an operative mortality of 1·88%. The operations performed were as follows: (1) pneumonectomy—118 cases, 3 early and 2 late deaths; (2) lobectomy—81 cases, no deaths; (3) segmental resection—50 cases, 1 early death; (4) bilateral segmental resection—4 cases, no deaths; and (5) wedge resection and spleliectomy—13 cases, 1 early death. After periods ranging from 3 months to 5 years, 247 patients (95%) are well and sputum-negative; 160 of these are working, 68 are at home, and 19 awaiting discharge from hospital.

The chief complications encountered were major haemorrhage (2), spread of disease (6 cases following lobectomy and 1 following pneumonectomy—all cleared with streptomycin and PAS), alveolar leaks (15), bronchopleural fistula (8), empyema (5), and reactivation of disease (7).

[This is an important paper and should be read in full by thoracic physicians and surgeons.]

F. J. Sambrook Gowar

993. **An Analytic Review of Excisional Surgery for Pulmonary Tuberculosis**

L. R. DAVIDSON, H. ALEXANDER, G. J. LUSTIG, B. J. KESNER, S. STERN, and A. E. BLOOMBERG. *Diseases of the Chest* [*Dis. Chest*] **25**, 262–277, March, 1954. 8 refs.

Between 1944 and 1952, at Sea View Hospital, Staten Island, New York, pulmonary excision was carried out on 487 patients, the total of 512 operations including pneumonectomy (333), lobectomy (150), and segmental resection (29). Half of the patients were negroes. The most frequent non-tuberculous conditions complicating the pulmonary disease were syphilis (32 cases), diabetes (19), and asthma (6). The authors emphasize that in many of the patients the disease was bilateral and was classified as "advanced". In all except the first 24 cases streptomycin was given during treatment.

The operative mortality was 15·4%, most of the 75 deaths being due to bronchopulmonary fistula with empyema and to haemorrhage and shock. Deaths from all causes totalled 97. The mortality rate was about the same for white patients as for negroes. Altogether 82 patients developed a bronchopulmonary fistula, but in 30 it was successfully closed. The death rate and the incidence of fistula increased with age. Contrary to expectation, mortality and the incidence of complications were slightly lower in diabetics (average age 44·3 years)

than in non-diabetics. The over-all mortality in patients of 50 years and over was 33·3%. Women in whom excisional surgery had been carried out appeared to tolerate pregnancy quite well.

Of the 390 patients who survived 331 were followed up, and of these 298 were well with a negative sputum, over half of them being fully active. Active pulmonary disease was still present in 15, and 18 had bronchopulmonary fistula, empyema, or wound infection.

The authors believe that still better results will be forthcoming in the future. The details of this investigation are analysed in several tables. *Paul B. Woolley*

994. **Comparative Study of Pulmonary Function Loss: Thoracoplasty versus Small Resection in Surgery of Tuberculosis**

F. B. LANDIS and W. WEISEL. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **27**, 336–348, April, 1954. 9 figs., 11 refs.

The loss of pulmonary function after limited apical thoracoplasty was compared with that following segmental resection and sub-segmental or wedge resection in patients at the Veterans Administration Hospital, Wood, Wisconsin. Of 71 patients, 24 underwent 5- or 6-rib thoracoplasty and 47 resection (segmental in 20 and sub-segmental or wedge in 27). Pulmonary function was assessed 2 weeks before operation and 3 months after resection and 6 months after thoracoplasty. A Collin respirometer and a Douglas bag were used to determine lung volume, maximum breathing capacity, and walking ventilation. In most cases bronchospirometry was also carried out.

The mean loss in total vital capacity was as follows: after thoracoplasty 25·4%; after segmental resection 11·1%; and after wedge resection 8·2%. Maximum breathing capacity was reduced by 11·3% after thoracoplasty, 5·5% after segmental resection, and 3·9% after wedge resection.

It thus appears that the functional loss after segmental resection is roughly one-half, and after wedge resection one-third, of that observed after limited thoracoplasty.

F. J. Sambrook Gowar

995. **A Comparison of Thoracoplasty and Resection Therapy in Pulmonary Tuberculosis**

T. G. BAFFES, P. SCHLOTTERBECK, and P. T. DECAMP. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **27**, 349–360, April, 1954. 11 figs., 10 refs.

Between 1942 and 1947 a total of 474 major operations were performed on patients with pulmonary tuberculosis at the Charity Hospital of Louisiana, New Orleans, including thoracoplasty on 321, lobectomy on 81 (segmental resection in 5), and pneumonectomy on 72. About half the patients subjected to thoracoplasty were operated on before 1947—that is, before streptomycin became available—whereas almost all those undergoing resection were operated on after that time. The race and sex distribution was 307 white and 167 coloured patients, and 244 males and 230 females. In 64% of the cases the disease was far advanced, in 35% moderately advanced, and in 1% minimal. Bilateral disease was present in 60% and cavitation in 86%. Before 1947 staged thoracoplasty was the operation usually employed, but since that time resection has been performed with increasing frequency, although many of the cases were suitable for thoracoplasty.

The operative mortality was 7·4% and the failure rate (including immediate postoperative deaths, later deaths, and cases in which the disease continued to be active) was 21·8%. In 336 cases (70·8%) the disease was arrested. The mortality in the immediate postoperative period among patients subjected to thoracoplasty (7·5%) was almost the same as that among patients undergoing resection (7·4%); further analysis of the latter group showed that mortality following lobectomy and pneumonectomy was 4% and 11% respectively.

The chief factors influencing the results were race, operative risk, and the date at which the operation was performed—that is, whether before or after the introduction of streptomycin therapy. Before 1947 the operative mortality was 40% in coloured patients and 8% in white patients, and the recovery rate was 40% and 62% respectively. After 1947 the mortality fell to 6% in coloured patients and to 5% in white patients, while the percentages of patients who recovered rose to 71 and 79 respectively.

The authors conclude that there is little to choose between thoracoplasty and resection on the basis of operative mortality, postoperative complications, and end-results, and that the character of the disease, the general condition of the patient, and the pre- and postoperative care influence the results of surgery to a greater extent than the type of operation carried out.

F. J. Sambrook Gowar

996. **The Relation of Amyloid Formation to the Type and Duration of Pulmonary Tuberculosis.** (Beitrag zur Abhängigkeit der Amyloidentstehung von Charakter und Dauer der Lungentuberkulose)

H. HAMKE and W. EDELHOFF. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **110**, 531–537, 1954. 3 figs., 19 refs.

In a study of 13 cases of pulmonary tuberculosis in which amyloidosis was diagnosed clinically and confirmed by the Congo-red test of Bennhold, the patients could be divided into two distinct groups on the grounds of constitutional type and reactivity of vegetative functions to physical, toxic, and psychic stimuli. These two groups were also found to differ in the nature and duration of the tuberculous process. Thus in 7 patients of the hyperreactive type (as indicated by dermographism, lability of temperature, and circulatory instability) the tuberculous lesions were of less than 5 years' duration, the disease process in general being progressive and exudative, with cavity formation, whereas in the remaining 6 patients, who were of the hyporeactive type, the tuberculous lesions were of more than 6 years' duration, the disease being mainly productive and fibrotic.

Investigations of protein metabolism in these cases largely confirmed the findings of other authors. Marked proteinuria was present in 6 cases. The total serum protein content was normal except where there was

nephrosis, when it was reduced, but the serum albumin concentration was generally below normal and those of α and β globulin above. However, the results of liver function tests (Takata–Ara, Mancke–Sommer, thymol turbidity, cadmium sulphate, and Weltmann coagulation tests) showed no characteristic changes. In one case clinical improvement was accompanied by a fall in the erythrocyte sedimentation rate and congo-red retention and an improvement in the results of the liver function tests and serum protein levels. *M. Lubran*

997. **Tuberculin Anergy and Secondary Pulmonary Tuberculosis in Cirrhosis of the Liver.** (L'anergie tuberculinique et la tuberculose pulmonaire secondaire des cirrhotiques)
R. Poinso and M. David. *Presse médicale* [*Presse méd.*] **62**, 580–581, April 17, 1954. Bibliography.

In a series of 80 patients with cirrhosis of the liver the authors found that 62 (77·5%) gave a positive skin reaction to tuberculin, while 3 others had active, bacteriologically proven tuberculosis. It is concluded that anergy to tuberculin is uncommon in cirrhotics, and that such anergy, when present, is related to the patient's poor general health and is not specific to the liver disorder. In only 5 of the 80 cirrhotic patients did manifest pulmonary tuberculosis develop, suggesting that the incidence of this complication is low and that it is not higher than in other chronic debilitating disorders.

[Apart from the three active cases mentioned, no evidence of present or past tuberculosis in the tuberculin-negative patients is presented, and it therefore cannot be asserted that their poor general condition was responsible for their negative tuberculin reaction—they may never have had tuberculosis. The incidence of pulmonary tuberculosis in comparable control groups was not determined and therefore the conclusions in this respect are also not necessarily valid.] *J. Lorber*

998. **The Incidence of Saprophytic Infestation with *Candida* in Cases of Pulmonary Tuberculosis.** (Sur la fréquence des infestations saprophytiques à *Candida* chez les tuberculeux pulmonaires)
J. A. Rioux, P. Verdier, and J. Plane. *Poumon* [*Poumon*] **10**, 101–106, Feb., 1954. 13 refs.

The authors draw attention to the marked increase of pulmonary infection with *Candida albicans* occurring during antibiotic therapy, especially in cases treated with aureomycin, chloramphenicol, penicillin, and isoniazid. The possible mechanism of action of these antibiotics in favouring the growth of *Candida albicans* is discussed.

In view of this they have investigated the incidence of *Candida albicans* in the sputum of a group of 266 patients (130 male and 136 female) with pulmonary tuberculosis at three sanatoria in the Montpellier region, some of whom had been given streptomycin. The sputum obtained after washing out the mouth with dilute Dakin's solution was inoculated on to Sabouraud's medium and the culture isolated.

It was found that 24·3% of all patients were infected with *Candida albicans*, the distribution being equal among the sexes, compared with a reported incidence of 14% of *Candida* infection in normal healthy adults. Of the 82 patients in one sanatorium, 43% of those whose sputum was positive for tubercle bacilli gave a culture of *Candida* compared with only 29% of those with negative sputum. Of the patients receiving streptomycin, 44% showed *Candida* in the sputum, against 31% of those not being treated with streptomycin. The authors consider, however, that the slight predominance in those treated with streptomycin can be explained by the more serious nature of the cases treated with that antibiotic, and consider that streptomycin, unlike aureomycin and chloramphenicol, does not promote the growth of *Candida albicans*. *G. M. Little*

999. **Diaphragmatic Pneumocele Complicating Therapeutic Pneumoperitoneum. A Review and Report of Four Cases**
R. L. Guillaudeu and D. B. Stewart. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 745–758, May, 1954. 6 figs., 18 refs.

TUBERCULOUS MENINGITIS

1000. **Electrolyte Imbalance in Tuberculous Meningitis**
S. A. Doxiadis, M. K. Goldfinch, and M. G. Philpott. *British Medical Journal* [*Brit. med. J.*] **1**, 1406–1410, June 19, 1954. 2 figs., 12 refs.

A low concentration of chloride in the cerebrospinal fluid has often been stressed as a valuable diagnostic feature in tuberculous meningitis, but the authors believe that this finding is not specific for the disease and merely reflects the depletion of the plasma chloride content caused by vomiting. At the University of Sheffield they studied the electrolyte balance of 19 children with tuberculous meningitis and of 2 with miliary tuberculosis without meningitis. Of 10 children with meningitis of 11 days' to 4 months' duration who had been vomiting during the previous fortnight (6 with papilloedema), all had hypochloraemia (plasma chloride 82 to 92 mEq. per litre), hyponatraemia (serum sodium 124 to 140 mEq. per litre), and plasma carbon dioxide levels of 20·5 to 34 mEq. per litre. Random specimens of urine still contained 18 to 123 mEq. of chloride per litre. In all of the 9 children who had had tuberculous meningitis for 3 to 28 months and who were not vomiting the electrolyte values were normal, as were they also in the 2 children with miliary tuberculosis, who vomited only occasionally. Of 7 of the cases of hypochloraemia in which electrolyte balance estimations were repeated, improvement occurred in 6 as vomiting ceased, although no persistent attempt had been made to correct the electrolyte imbalance. In 2 of these patients hydrocephalus was still present after the electrolyte values had returned to normal.

During treatment 4 of the hypochloraemic children and the 2 control patients were given approximately 2 ml. of 15% saline per kg. body weight intravenously. Within an hour the plasma chloride and serum sodium levels had risen, but they fell rapidly in all but one moribund,

anuric child. To 2 of the other hypochloraemic children 109 to 143 mEq. of potassium was given by mouth for 4 or 5 days. One child with a low serum sodium level retained only 26% of this load, whereas the other, whose serum sodium level was normal, retained 81%.

The authors conclude that reduced food intake and vomiting can account for the electrolyte disturbances in patients with tuberculous meningitis, and that maintenance of adequate electrolyte intake in the early stages may contribute towards recovery. *Thomas B. Begg*

1001. **Tuberculous Meningitis in Children Treated with Streptomycin and P.A.S.**

J. LORBER. *Lancet* [*Lancet*] **1**, 1104–1107, May 29, 1954. 11 refs.

The treatment of patients suffering from tuberculous meningitis has become progressively more effective since 1947, when streptomycin first became available. In the initial stage, when the potentialities of streptomycin were as yet undetermined, the Medical Research Council organized a trial at three centres in the British Isles and the results were most encouraging. From 1948 to 1950, when streptomycin was used more widely, standardized methods of treatment were adopted and additional measures such as the intrathecal injection of tuberculin were employed. The third phase began when PAS was given with streptomycin, and the fourth phase was marked by the use of isoniazid. The author presents the results obtained during the third of these therapeutic phases at the Children's Hospital, Sheffield, and compares them with his own (and those of other workers) in the second phase.

In all, 38 children with tuberculous meningitis were admitted between August, 1950, and March, 1952, and they have been followed up for at least 2 years; 26 were boys, 14 were under the age of 3, and only 2 were over 10. On the basis of the Medical Research Council's classification, 25 were in the early or intermediate stages of the disease, and nearly one-third were in the advanced stage and unconscious; 12 had meningitis with miliary tuberculosis. Streptomycin was given intramuscularly in a dosage of 10 mg. per lb. (22 mg. per kg.) body weight twice daily for at least 6 months, streptomycin intrathecally in a dose of 25 to 50 mg. was given with occasional rest days for 45 injections, and PAS was given by mouth in a dosage of 0·5 g. per kg. per day from the beginning of treatment and for about 3 months after intramuscular streptomycin had been discontinued. Also 12 selected patients were given intrathecal tuberculin (P.P.D.) and 3 received intrathecal streptokinase.

The 2-year survival rate was 73·7% (28 patients), a figure about 25% higher than the survival rates at 5 major English centres for the period 1947 to 1950 (that is, before PAS was available). Of 3 children who became deaf or partially deaf, all had received intrathecal injections of streptomycin for a prolonged period. One child became partially blind, and 2 patients relapsed after completion of streptomycin therapy. Compared with previous experience at Sheffield it is apparent that with the addition of PAS the duration of intramuscular streptomycin therapy became shorter, fewer intrathecal injections of streptomycin were required, and the incidence of spinal block and of relapses became less. Altogether 75% of the survivors were free from any sequelae, as compared with 61% in the previous series.

The importance of early diagnosis and its effect in prognosis was obvious, 92·6% of the children who were in the early stages, as evidenced by consciousness, on admission recovering. The presence of miliary tuberculosis did not appear to affect the prognosis. Although prognosis was poorer in the younger patients, analysis of the results showed that this was because the younger children were in a more advanced stage of the disease when admitted for treatment.

[Isoniazid was not given to these patients, but preliminary reports from centres in Britain and the U.S.A. suggest that it may be possible to dispense with the intrathecal injection of streptomycin, since the results with intramuscular streptomycin and oral isoniazid are as good as, or better than, those in the present series.]

R. M. Todd

1002. **Isoniazid and Streptomycin in Tuberculous Meningitis**

J. LORBER. *Lancet* [*Lancet*] **1**, 1149–1151, June 5, 1954. 1 ref.

In a previous paper [see Abstract 1001] the author reported excellent results in the treatment of tuberculous meningitis with intramuscular and intrathecal streptomycin and oral PAS (together with intrathecal tuberculin (P.P.D.) in selected cases). During a period of 20 months 25 patients survived out of 27 who were conscious on admission, and 3 out of 11 who were unconscious, the total rate of survival being 73·7%. He now reports the results obtained with the same plan of treatment but with the addition of oral isoniazid. Between April, 1952, and August, 1953, 27 patients with tuberculous meningitis were treated, 5 being unconscious on admission and 22 conscious. In all but one case tubercle bacilli were found in the cerebrospinal fluid (C.S.F.). All were given streptomycin intramuscularly and PAS by mouth for at least 6 months and at least one course of 45 intrathecal injections of streptomycin. In addition, all the unconscious patients and 12 of the conscious patients were given isoniazid by mouth in doses of 5 mg. (later increased to 20 mg.) per kg. body weight daily for at least 6 months.

No significant difference in survival rate was found. Of the 5 unconscious patients, 2 survived; of the 12 conscious patients treated with isoniazid, 11 survived; and of the 10 treated without isoniazid, 8 survived, the total survival rate being 78·5%. However, the patients receiving isoniazid required much less intrathecal streptomycin—an average of 65 injections per case compared with 90 for those not receiving isoniazid. Moreover, the cell count in the C.S.F. improved more rapidly with isoniazid, although in 6 cases a second course of intrathecal streptomycin treatment was required because the C.S.F. cell count showed deterioration after the first course, tubercle bacilli reappearing in one case.

These observations lead the author to conclude that although isoniazid is a valuable addition to the drugs

hitherto used in tuberculous meningitis, intrathecal streptomycin is still needed. He points out, however, that no controlled investigation appears to have been reported in which the results, in concurrent series of similar cases, of treatment with systemic streptomycin and isoniazid, with and without intrathecal streptomycin, have been compared. *A. W. Franklin*

1003. **The Blood–C.S.F. Barrier to Bromide in Diagnosis of Tuberculous Meningitis**
L. M. TAYLOR, H. V. SMITH, and G. HUNTER. *Lancet* [*Lancet*] **1**, 700–702, April 3, 1954. 3 figs., 6 refs.

It is now established that the overriding factor in the prognosis of tuberculous meningitis is the stage which the disease has reached at the time treatment is begun. In a series of 80 cases treated at the Radcliffe Infirmary, Oxford, between December, 1949, and July, 1952, whereas the over-all mortality was 37·5%, no patient died among those 21 who were still fully conscious and rational and without focal neurological signs when treatment was begun. Yet it is precisely at this stage of the disease, when treatment is most efficacious, that diagnosis can be most difficult, and as a result these favourable cases remain a small minority of the whole. When evidence of systemic tuberculosis is lacking the clinical picture at this stage of the illness is simply one of mild meningeal inflammation. The abnormal findings in the cerebrospinal fluid may be limited to a lymphocytic pleocytosis and some increase in the protein content, since the chloride content is seldom decreased, and not infrequently even the glucose content is still within normal limits.

The authors have received a considerable amount of help in the diagnosis of these difficult cases from the results of studies of the passage of bromide from the blood to the cerebrospinal fluid (C.S.F.). It has been found that in normal subjects with no detectable disease of the nervous system the serum contains 2 or 3 times as much bromide as the C.S.F. following a test dose of sodium bromide—in other words, the serum : C.S.F. bromide content ratio is 2 or 3 to 1. There is a steady fall in the bromide ratio following the introduction of tuberculin into the C.S.F. of a Mantoux-positive person with normal meninges and without active tuberculosis. Active tuberculous meningitis appears to have the same effect, and the ratio falls early in the illness.

In other varieties of non-purulent meningitis a fall in the bromide ratio comparable with that occurring in tuberculous meningitis has only exceptionally been found. In such cases, even though the changes in the number of cells and the amount of protein in the C.S.F. were about the same as those in tuberculous meningitis, the blood–C.S.F. barrier to bromide was, on the whole, remarkably well maintained. In the great majority of 33 of the authors' cases of tuberculous meningitis the bromide ratio was between 0·7 and 1·29, and in only 3 cases was it higher than 1·6. In 33 cases of non-tuberculous, non-purulent meningitis the ratio distribution showed a flatter peak—as might be expected in a group of mixed aetiology—but in only 2 of these 33 cases was the ratio lower than 1·6. Thus, taking a ratio of 1·6 as the critical level, in only 5 cases out of 66 was the ratio above or below the expected figure, giving an error of approximately 7%.

The authors therefore conclude that the determination of the permeability of the blood–C.S.F. barrier for bromide may be helpful in the early diagnosis of tuberculous meningitis, and in its differential diagnosis from other forms of meningitis. *J. MacD. Holmes*

1004. **Subclinical Forms of Tuberculous Meningitis.** (Le forme sub-cliniche della meningite tubercolare)
A. GENTILI and A. PACI. *Minerva pediatrica* [*Minerva pediat. (Torino)*] **6**, 265–275, April 30, 1954. Bibliography.

It has been the authors' experience at the Paediatric Clinic of the University of Pisa that tuberculous meningitis is frequently well established before any clinical evidence of its presence is forthcoming, examination of the cerebrospinal fluid often providing the earliest indication of meningeal involvement in such cases. They describe briefly 26 cases of tuberculous meningitis in children, in 13 of which the history, signs, and symptoms did not give rise to any suspicion of meningitis until lumbar puncture was performed. In the other 13 cases there were indications of meningeal involvement, such as headache, restlessness, and nuchal stiffness, but these were relatively mild and arose weeks or even months after some febrile episode.

The majority of the children were seen originally with signs of respiratory disease or alimentary disorder not in themselves suggestive of tuberculosis. They were admitted to the clinic because they were not thriving, but routine lumbar puncture revealed the presence of active meningitis. The authors point out that even if tuberculosis had been suspected in these cases it would have been regarded as respiratory or alimentary and treatment in that event would probably have been insufficient to clear the meningitis. Furthermore, such treatment may delay the onset of meningitis by inhibiting, although only partially, the invasion of the meninges. In some cases meningitis may be suspected in a child in whom the lack of growth and persistence of fever seem disproportionate to the pulmonary condition, or possibly where there is a positive tuberculin reaction without definite signs of tuberculosis.

The authors are convinced that the condition of subclinical tuberculous meningitis is a real clinical entity. Whether it remains subclinical depends mainly on four factors: the extent and degree of meningeal invasion, the period elapsing between invasion and recognition of the condition, the intensity of treatment, and virulence of the causal organism; the first and the last factors seem to play the greatest part in the production of the subclinical forms. Finally, the authors point out that, although meningitis can be diagnosed in these cases only by lumbar puncture, and even then not always with certainty, adequate therapy in all cases of tuberculosis should prevent the appearance of clinical signs of meningitis, even after invasion of the meninges, and cure is possible without any apparent involvement of the nervous system. *J. G. Jamieson*

See also Bacteriology, Abstracts 944–5.

Venereal Diseases

1005. **Studies with the Treponemal Immobilizing Test**
J. L. MILLER, M. H. SLATKIN, M. BRODEY, H. L. WECHSLER, and J. H. HILL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **154**, 1241–1247, April 10, 1954. 1 fig., 15 refs.

In this paper from Columbia University and the Presbyterian Hospital, New York, the results are given of a comparative investigation of the treponemal immobilization (T.P.I.) test and three standard serum tests for syphilis—the Mazzini, the V.D.R.L., and the Kolmer tests. In the first investigation sera from 17 patients with early syphilis, 30 with early latent syphilis, 139 with late latent syphilis, 38 with neurosyphilis, and 7 with cardiovascular syphilis were examined. With the exception of 9 cases of early syphilis which had been treated 9 to 40 years previously, the T.P.I. test gave a positive reaction in all cases. It also gave a positive result with the cerebrospinal fluid of all of the 38 patients with neurosyphilis, whereas the standard tests were positive in only 26 of these cases.

Sera were also examined from a group of 162 patients who presented diagnostic problems. The diagnosis of syphilis was based on evidence other than the serological findings in only 14 of these cases; the T.P.I. reaction was positive in all these 14, and in the whole group it was positive in 72 and negative in 90. Of these 90 patients in whom the result was negative, 59 had received treatment for syphilis.

Parallel tests were carried out on selected patients admitted to hospital for a wide range of conditions other than syphilis, in many of whom the standard tests had given positive results. Among these, of 14 patients with acute disseminated lupus erythematosus, 11 had positive or weakly positive reactions to the standard tests, whereas that to the T.P.I. test was negative in 12, and in 2 cases the serum was too anticomplementary for a satisfactory test to be carried out. Of 4 patients with subacute disseminated lupus erythematosus, the standard tests gave positive or weakly positive reactions in 3 and the T.P.I. test in only one. Again, the standard tests gave positive results in 4 cases of discoid lupus erythematosus, and the T.P.I. test in only 2 of these. On the other hand, of 12 patients with sarcoidosis, 11 gave a positive or weakly positive response to the standard tests and 10 to the T.P.I. test.

Evidence of the passive transfer of immobilizing antibody through the placenta was obtained on examination of 93 babies born of 74 mothers who had received varying types of treatment before or during pregnancy, of whom 55 had latent syphilis, 11 congenital syphilis, and 4 early syphilis; of the remainder, one had had yaws and 3 had given non-specific reactions. Only one baby showed signs of active syphilis, and its mother developed secondary syphilis post partum. Serial T.P.I. tests on 70 babies showed that while the passively transferred reagin disappeared from the child's blood by the 3rd month in 91% of cases, the immobilizing antibody persisted until the 4th or 5th month, usually disappearing by the 6th month.

The authors conclude that despite the diagnostic value of the T.P.I. test, it cannot be used as a guide to treatment, since no amount of treatment seems to alter it in patients who have not been adequately treated early in the infection. The test remains, however, the only practical procedure available for separating the group of false positive reactors from patients with latent syphilis. It is the authors' opinion that no one of the standard tests used is more valuable than any other in the diagnosis of syphilis, and that a high-titre reaction to the standard tests is not necessarily an indication of its specificity, since such reactions may be given by patients known to be false positive reactors. The T.P.I. test is especially helpful in the diagnosis of neurosyphilis, since the cerebrospinal fluid gives positive reactions in both the symptomatic and asymptomatic forms unless treatment has been given very early in the disease.

[This paper does not readily lend itself to abstracting because of the wide diversity of the clinical material studied, and should be read in the original by all those interested.] *A. E. Wilkinson*

1006. **The Treatment of Gonorrhoea with Streptomycin.**
(Zur Behandlung der Gonorrhöe mit Streptomycin)
P. ZIERZ and R. JACOB. *Hautarzt* [*Hautarzt*] **5**, 223–227, May, 1954. 1 fig., 35 refs.

The authors discuss the reasons which have prompted some workers to replace penicillin by streptomycin and other antibiotics in the treatment of gonorrhoea. These reasons have included the alleged frequent development of resistance to penicillin, the relative frequency of post-gonorrhoeal urethritis after treatment with the drug, and also the danger of masking the presence of associated syphilis, and it has been claimed that streptomycin is as efficacious as penicillin but without its disadvantages.

In a study undertaken by the authors at the University Dermatological Clinic, Heidelberg, to test this claim, 23 proved cases of gonorrhoea were treated with dihydrostreptomycin in doses of 0·5 g. once or twice daily or 1 g. once daily. The treatment failed completely in 4 cases owing to rapid development of resistance, but in the others serological reactions remained negative for 3 to 5 months after treatment.

The authors consider that the development of resistance to streptomycin is probably due to mutant strains, and is a serious disadvantage of this form of treatment. One strain in the series treated which became resistant to streptomycin was also sensitive to penicillin, aureomycin, and sulphadiazine, and its resistance could not be diminished by the addition of a sub-optimal concentration of penicillin. They conclude that although streptomycin is no doubt extremely effective against the gonococcus, its use in the treatment of gonorrhoea cannot be recommended because of the rapid development of resistance. *Ferdinand Hillman*

Tropical Medicine

1007. **An Experiment in the Control of Schistosomiasis. First Report**
G. MACLEAN and U. HAY. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **48**, 21–27, March, 1954. 3 refs.

An experiment in schistosomiasis control was carried out on Likoma, an island in Lake Nyasa, Africa, with a resident population of 3,600. After instruction of the inhabitants in the causation and prevention of the disease, an attempt was made to poison the snails which are the vectors by treating a frequently-used strip of the lake shore with copper sulphate. The minimum concentrations aimed at were 1 in 100,000 in stagnant pools and 10 grains per sq. foot (7 g. per sq. m.) where the water was less than 1 foot (30 cm.) deep. Frequent application was necessary, and the number of snails was greatly reduced, but complete elimination was not possible. Finally, mass treatment of the 957 cases of genito-urinary schistosomiasis in the population was carried out by administration of "nilodin" (lucanthone hydrochloride) in total dosage of 30 mg. per lb. body weight (66 mg. per kg.) over a period of 3 to 5 days. Of 801 patients followed up, 45 were still infected. Further follow-up examinations were planned and the experiment is being continued. *J. L. Markson*

1008. **Arsenamide Treatment of Filariasis due to *W. bancrofti* and *A. perstans***
J. A. MCFADZEAN and F. HAWKING. *British Medical Journal* [*Brit. med. J.*] **1**, 956–959, April 24, 1954. 11 refs.

"Arsenamide", *p*-bis-(carboxymethyl mercapto)-arsinobenzamide, a tervalent arsenical, has been used by a number of workers in the treatment of filariasis since 1948, and was previously tried in cases of sleeping sickness.

The present authors describe the results obtained in the treatment with this drug of 37 cases of filariasis due to *Wuchereria bancrofti* in Gambia, British West Africa. The dose in 32 cases was 1·8 to 2·5 mg. per kg. body weight daily by intravenous injection, usually for 10 to 12 days, and in the other 5 cases 0·3 mg. per kg. daily for 14 days.

In the higher dosage treatment was very effective, most of the microfilariae of *W. bancrofti* being removed from the blood within 2 weeks of the first dose of arsenamide and all but 2 patients being still free from microfilariae 6 months later. Moreover, there was also a reduction in the number of microfilariae of *Acanthocheilonema perstans* present. Even with the lower dosage the microfilaria count was significantly reduced in 4 out of the 5 cases, it being estimated that the minimum curative dose is probably about 0·6 mg. per kg. Minor toxic symptoms included vomiting, dizziness, headache, loss of weight, and possibly diarrhoea, while allergic reactions due to the death of adult worms occurred in a few patients. By far the most serious toxic effect of the drug, however, was on the liver; jaundice occurred in 2 cases, and one patient developed fatal necrosis of the liver after having received only 3 injections.

The authors therefore consider that since filariasis is not a fatal disease it is not justifiable to use arsenamide except in special circumstances, when care should be taken to avoid damage to the liver by the use of small doses and enrichment of the diet with extra protein.
R. Wien

1009. **Further Observations on Intravenous Chloramphenicol in Cholera**
H. S. CHAKRAVARTI, A. MONDAL, A. M. MUKHERJEE, and N. G. PAL. *Journal of the Indian Medical Association* [*J. Indian med. Ass.*] **23**, 331–332, May, 1954. 4 refs.

The results of the treatment of cholera with chloramphenicol given intravenously in 50 cases are compared with those in 50 control cases. Both groups received the usual saline treatment. The chloramphenicol was given in saline or glucose solution, 0·5 g. on admission and 0·25 or 0·5 g. every 4 hours subsequently [but the total period of treatment is not specified]. The stools became formed and vibrios disappeared sooner in the treated group than in the control group, but otherwise there was no significant difference between them. The earlier sterilization of the stools, as the authors note, has some value from the public-health point of view.
William Hughes

1010. **The Middlebrook–Dubos Reaction in Leprosy.** (La reazione di Middlebrook–Dubos nella lepra)
L. LUCENTINI and P. NAZZARO. *Annali italiani di dermatologia e sifilografia* [*Ann. ital. Derm. Sif.*] **9**, 97–100, March–April, 1954.

During a study, carried out at the University of Rome, of the Middlebrook–Dubos reaction in a variety of tuberculous and non-tuberculous conditions, a high positive titre was obtained in several cases of leprosy, and further investigations have accordingly been made on a larger group of patients with this disease. The original technique as modified later by Middlebrook was used, the antigen being obtained from the Pasteur Institute in Paris.

Altogether, the test was carried out in 27 cases of leprosy. Of 18 cases of cutaneous leprosy a positive reaction was obtained in 17, the titre in 15 being 1:128. In both of 2 cases of cutaneous leprosy during remission a positive titre of 1:128 was obtained. Of 3 cases of nervous leprosy, only one gave a positive reaction, with a titre of 1:32. In all of 4 cases of mixed leprosy the reaction was positive, in 3 of them with a titre of 1:128.

The authors briefly discuss the similar findings of other workers in this field. The positive reaction so consistently obtained in cases of leprosy not only emphasizes its similarity to tuberculosis, but may also be of value in diagnosis. *R. F. Jennison*

Allergy

1011. **Incidence of Allergic Diseases in General Practice**
N. J. T. HAMILTON and B. BENDKOWSKI. *British Medical Journal* [*Brit. med. J.*] **1**, 1069–1070, May 8, 1954. 12 refs.

In an industrial practice in the north-west of England the incidence over a period of one year of five common allergic disorders was studied. The number of patients on the list of the practice was about 4,000. The total of 209 allergic cases seen during the period was made up as follows: asthma, 68 cases; urticaria, 72; allergic rhinitis, 30; atopic eczema, 27; and drug allergy, 12. Of the 68 patients with asthma (1·7% of the total number of patients on the list of the practice), 45 were of working age (from 20 to 70 years). Details of the diagnosis, age at onset of the disease, and duration of symptoms are given, special reference being made to drugs causing allergic manifestations.

The authors consider that while the figures may not indicate the actual incidence of these allergic conditions in Britain, they are representative of that section of the population who attend the average surgery for these disorders. *A. W. Frankland*

1012. **The Measurement of Resistance to Air Flow in the Human Bronchial Tree.** (Die Bestimmung des Strömungswiderstandes im Bronchialsystem des Menschen)
K. JEKER. *Helvetica medica acta* [*Helv. med. Acta*] **20**, 459–489, Dec., 1953. 13 figs., 45 refs.

The [unorthodox] views on bronchial resistance to air flow held by the author and his colleagues at the University of Berne are reviewed in detail. Bronchial resistance is calculated from alveolar pressure and air flow, the former being determined by occlusion of the airway for a period of 0·1 second by means of a fast-closing shutter, or by measuring oesophageal pressure, the latter by means of a pneumotachograph. The bronchial resistance of patients with asthma is stated to be about double that of normal subjects. This comparatively small increase in resistance, which sometimes occurs also in normal subjects during nasal breathing, is insufficient to account for the breathing difficulty in asthma, the greater part of which is attributed to factors outside the bronchi—namely, the failure of the diaphragm and the thoracic muscles to supply the necessary expiratory force.

Evidence in support of this view is provided by estimations of the rate of air flow during a maximum expiratory effort by means of a pneumometer; in the asthmatic subject the inhalation of an antispasmodic aerosol (such as isoprenaline) quickly reduces bronchial resistance to normal, whereas the pneumometer value, which is dependent on both bronchial and extrabronchial resistance, is only partially reduced. Artificial stenosis of the air passages in the normal subject does not affect the pneumometer value until the bronchial resistance is more than double the normal, and it is calculated that to increase the pneumometer value to the levels observed in asthmatics would require a degree of stenosis causing a twentyfold increase in bronchial resistance.

[Like so many unorthodox views, the suggestion that bronchial spasm or bronchial obstruction is a minor factor in the mechanism of bronchial asthma is stimulating. It may be that in asthmatics with well-developed temporary inflation of the thorax the muscles involved develop a state of contraction which prevents them from carrying out their normal expiratory activity—if any. Nevertheless, there are numerous experimental observations on bronchial function which make it difficult to accept the author's view.] *H. Herxheimer*

1013. **Collective Asthma, Simulating an Epidemic, Provoked by Castor-bean Dust**
E. MENDES and A. ULHÔA CINTRA. *Journal of Allergy* [*J. Allergy*] **25**, 253–259, May, 1954. 7 refs.

In this paper from the University of São Paulo, Brazil, the authors describe how in August, 1952, 150 persons fell ill of an apparently epidemic disease with the symptoms of bronchial asthma in Baurú, a Brazilian town of some 60,000 inhabitants. These cases all occurred within a period of a few days shortly after a large mill producing castor oil and castor-bean pomace had changed its extraction process. When the mill resumed work after being inactive for about one month a new outbreak occurred, but no new cases appeared when it was closed down for one year. In all, 9 deaths were attributed to the illness.

Thirty patients were studied by the authors by means of cutaneous tests, passive-transfer tests, and bronchial tests, and it was established beyond doubt that the illness was bronchial asthma and allergic rhinitis provoked by castor-bean dust. Of the 30 patients, 12 had previously suffered from asthma; in 17 cases the symptoms disappeared when the patients moved temporarily to another town 15 km. distant, but reappeared on their return to Baurú. Many of the patients stated that the symptoms became less intense or disappeared when it rained.

[This report confirms the high antigenicity of castor-bean dust in man. A similar occurrence was reported by Figley and Elrod from a town in Ohio (*J. Amer. med. Ass.*, 1928, **90**, 79). They serve to show that allergization of an individual does not necessarily depend on his allergic disposition, but on the amount and antigenicity of the allergen with which he comes into contact. Possibly every individual can be allergized if these are great enough.] *H. Herxheimer*

1014. **The Use of Protein Skin Tests in the Celiac Syndrome**
C. COLLINS-WILLIAMS and J. H. EBBS. *Annals of Allergy* [*Ann. Allergy*] **12**, 237–240, May–June, 1954. 14 refs.

Nutrition and Metabolism

1015. **Clinical Usefulness of New Milk Protein Supplement**

G. H. MARQUARDT, G. M. CUMMINS, L. A. RIGGS, and C. I. FISHER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **154**, 1164–1167, April 3, 1954. 2 figs., 10 refs.

The preparation and clinical use of a new milk-protein supplement (" kralex ") are described. Skim milk is passed through ion exchange columns, thus reducing the mineral content and, incidentally, the vitamin content. It is then concentrated by evaporation, after which washed, freshly precipitated casein is added in an amount which doubles the protein content. The final product is either tinned in this concentrated liquid form or is spray-dried to a powder. In the liquid form one 6-oz. (170-ml.) tin supplies 24 g. of protein, 14 g. of carbohydrate, and an almost negligible amount of sodium (4 mg.). The preparation contains practically no iron or ascorbic or nicotinic acid, but reasonable amounts of riboflavin, aneurin, and some other vitamins of the B group.

This protein supplement was given to 5 patients at the Wesley Memorial Hospital, Chicago, in amounts which supplied up to 180 g. of protein daily. In 2 cases of chronic glomerulonephritis and one case of hepatic cirrhosis the serum protein level was low and there was extensive oedema; after administration of the protein supplement the serum protein level rose and the oedema became markedly less. In a case of obesity and one of rheumatic valvulitis with arteriosclerosis a normal serum protein level was maintained by administration of this preparation, which supplied not less than 90% of the dietary protein.

The advantages claimed for the new preparation are: (1) it contains all the essential amino acids; (2) it is palatable and can readily be taken as a drink with a variety of flavours or as a solid in puddings or in bread; (3) it is highly concentrated; (4) the sodium content is low; and (5) it is relatively cheap [the cost is not stated].

[It is difficult to see what advantage this preparation has over dried casein, which is already easily available. Indeed, the presence of lactose in an amount equal to more than half that of the protein may in some instances be a disadvantage.] *John Yudkin*

1016. **Basal Metabolism in Nutritional Edema**

P. S. VENKATACHALAM, S. G. SRIKANTIA, and C. GOPALAN. *Metabolism* [*Metabolism*] **3**, 138–141, March, 1954. 9 refs.

The changes in the basal metabolic rate (B.M.R.) in 10 patients with nutritional oedema, and the factors responsible, were studied at the Nutritional Research Laboratories, Indian Council of Medical Research, Coonoor. When the patients were admitted to hospital the B.M.R. was 20% below normal; after treatment it was higher than at the time of admission, but was still a little below normal, except in one case. The rise in the B.M.R. was accompanied by a reduction in the surface area of the body. The authors state that the fall in the B.M.R. was due almost entirely to a reduction in the amount of metabolizing tissue and not to a reduction in the oxygen consumption per unit of metabolizing tissue. *F. W. Chattaway*

1017. **The Electrocardiogram in Potassium Depletion. Its Relation to the Total Potassium Deficit and the Serum Concentration**

W. B. SCHWARTZ, H. D. LEVINE, and A. S. RELMAN. *American Journal of Medicine* [*Amer. J. Med.*] **16**, 395–403, March, 1954. 4 figs., 12 refs.

The relation between electrocardiographic changes and total potassium deficit and serum potassium concentration was analysed in 14 balance studies on 9 normal subjects in whom potassium depletion was produced by the administration of deoxycortone acetate, 17-hydroxycorticosterone acetate (Compound F), ammonium chloride, or ammonium sulphate, and on 2 patients with severe chronic potassium depletion induced by overuse of laxatives. None of these 11 subjects had any clinical evidence of cardiovascular disease. No consistent quantitative correlation was found between the state of the body potassium stores and the appearance of the electrocardiogram. Normal tracings were obtained in the presence of a low serum potassium level, while a normal serum concentration did not always prevent the development of characteristic electrocardiographic changes during potassium depletion.

It is concluded that " the electrocardiogram cannot be relied upon to indicate acute changes in body potassium stores even when these are large enough to be of clinical significance. Such electrocardiographic changes as do occur are not consistently related to the quantity of potassium gained or lost or to the serum potassium concentration, and the appearance of these alterations may be delayed one or more days. For these reasons it would appear hazardous to attempt to use the electrocardiogram as a daily guide to therapy of potassium depletion with potassium salts ".

[Although the numbers involved in this carefully planned study may be too small to allow of detailed statistical analysis, the findings must be given careful consideration and should act as a useful corrective to the recent tendency towards the uncritical use of the electrocardiogram in the management of patients with potassium depletion.] *William A. R. Thomson*

1018. **Diagnosis of Acute Porphyria**

E. G. SAINT, D. CURNOW, R. PATON, and J. B. STOKES. *British Medical Journal* [*Brit. med. J.*] **1**, 1182–1184, May 22, 1954. 13 refs.

Gastroenterology

1019. **Hiatus Hernia: the Problem of Diagnosis**
E. D. PALMER. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **27**, 271–276, March, 1954. 2 figs., 5 refs.

In discussing the problem of the diagnosis of hiatus hernia, the author observes that a clinical diagnosis of reflux oesophagitis is often not substantiated by the discovery of a hiatus hernia at *x*-ray examination. A comparative investigation was therefore undertaken to determine whether hiatus hernia could be more frequently discovered by other methods—namely, oesophagoscopy and gastroscopy.

It was found that radiology failed to demonstrate the lesion in 83 out of 159 examinations (52%) of subsequently proven cases. Even after the diagnosis had been established by other methods repeat radiographs still failed to show evidence of the hernia in about half of the remainder. Gastroscopy was even less dependable, revealing the lesion in only 19 out of 41 cases. Oesophagoscopy, on the other hand, disclosed or confirmed the presence of a hernia in 44 out of the 51 patients examined by this procedure. Two cases are illustrated in which at oesophagoscopy brain clips were placed at the site of biopsy taken below what appeared to be the cardia. These biopsy specimens were later shown to consist of gastric mucosa, although the radiographs seemed to show oesophageal mucosal patterns in the 4- to 6-cm. interval between the clips and the diaphragm. The author discusses the difficulty of distinguishing gastric from oesophageal mucosa by radiography, and the implications of this in regard to hiatus hernia.

[No figure is given for the number of patients in whom reflux oesophagitis or hiatus hernia had been diagnosed clinically, but in whom no hernia was later found by any of the three methods of examination.]

H. Daintree Johnson

1020. **Angular Stomatitis and its Association with Artificial Dentures**
J. G. HARKNESS. *British Medical Journal* [*Brit. med. J.*] **1**, 1415–1418, June 19, 1954. 2 refs.

The aetiological factors in 46 cases of angular stomatitis seen at the General Infirmary at Leeds are discussed. In only a few of the cases was the condition associated with infection, seborrhoeic eczema, or ariboflavinosis; in the majority the stomatitis was thought to be due to sensitization to denture materials. The reaction to a patch testing, in which a scraping from the patient's denture was held against the skin, was positive in a number of cases. In some instances the reaction was delayed for 96 hours, and it is therefore considered that the patch should be left *in situ* for not less than this period. The nature of the sensitizing material remains obscure. The condition cleared up in 18 of the 32 patients whose dentures were remade in a different material. Opening of the dental bite helped in some cases.

G. W. Csonka

1021. **The Comparative Sensitivity of the Mucosa of the Various Segments of the Alimentary Tract in the Dog to Acid-peptic Action**
L. B. KIRILUK and K. A. MERENDINO. *Surgery* [*Surgery*] **35**, 547–556, April, 1954. 2 figs., 9 refs.

In experiments carried out on dogs at the University of Washington School of Medicine, Seattle, to determine the relative susceptibility of the mucosa of different parts of the alimentary tract to gastric juice, the tract was exposed by a combined thoraco-abdominal incision and the wall of the oesophagus, stomach, duodenum, jejunum, and ileum incised to expose the mucosa of each. A solution (*p*H 1·2) containing 1% pepsin and 0·1 N hydrochloric acid was allowed to drip on each type of mucosa from a height of 2 in. (5 cm.) at the rate of 1 ml. per minute for periods ranging from 15 minutes to 15 hours. Three of the animals were killed at the end of the experiment and examined at once; the remaining 9 dogs were allowed to recover after surgical repair.

The area of gastric mucosa tested was rapidly covered by a layer of mucus and showed no sign of injury at all. The mucosa of the duodenum, jejunum, and ileum, which suffered about equal degrees of injury, showed the following changes: as soon as the drip was begun blanching occurred, followed by the formation of a layer of mucus; petechial haemorrhages occurred within 5 minutes; superficial necrosis of villi was seen in 15 and thrombosis of mucosal vessels in 30 minutes. After 15 hours there was severe damage to all layers of the bowel wall. Recovery from injury was rapid, however, for only 2 of the 9 dogs allowed to recover showed signs of injury at post-mortem examination; this was trivial in one of the animals, but in the other, killed at 72 hours after exposure to the drip for 60 minutes, ileal ulceration was found.

The stratified epithelium of the oesophagus suffered most damage. Within 15 minutes epithelial vessels were thrombosed, and after 30 minutes all the epithelium had disappeared. After exposure to the drip for 15 hours there was ulceration with oedema of the whole muscle layer. Of the group of animals which were allowed to recover, all showed ulceration of the oesophagus at later necropsy. Healing, however, was seen to be beginning after 3 days, but was not complete even after 15 days.

A. G. Parks

1022. **Periodic Peritonitis—Heredity and Pathology. Report of Seventy-two Cases**
H. A. REIMANN, J. MOADIÉ, S. SEMERDJIAN, and P. F. SAHYOUN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **154**, 1254–1259, April 10, 1954. 6 figs., 13 refs.

Periodic peritonitis is characterized by short episodes of pain in the abdomen and elsewhere, fever, and leucocytosis, which occur at regular or irregular intervals over many years. At Beirut, Lebanon, a total of 72 cases

was seen during a recent 5-year period; 49 of the patients were Armenians, who seem to be particularly susceptible. The condition appears to be familial; the authors describe and give the pedigree of one family of which 20 members in five generations were affected. A sterile, mild, non-suppurative inflammatory process, involving the walls of the appendix and the gall-bladder, was found in patients operated on during or between episodes. The underlying mechanism and the cause of the repetitive, uniform episodes are not known. *Harry Harris*

SALIVARY GLANDS

1023. **Differentiated Mucoepidermoid Tumors of Salivary Glands**

R. A. MARCIAL-ROJAS and S. C. SOMMERS. *Archives of Otolaryngology* [*Arch. Otolaryng. (Chicago)*] **59**, 135–140, Feb., 1954. 6 figs., 9 refs.

Accurate classification of tumours of the salivary glands is made difficult by the tendency of the epithelium of the acini and ducts to undergo metaplastic change. Thus squamous metaplasia is common in chronic sialadenitis and is found in atrophied glands and in tumours after *x*-ray treatment, and keratinization of the epithelium is found in Mikulicz's disease; while metaplasia of the stroma—myxomatous or cartilaginous change—also occurs. In part, at least, the mixed histological pattern of salivary-gland tumours is due to these metaplastic changes.

The present authors suggest that the term " mucoepidermoid tumour " should be used to describe " those slowly growing radiosensitive neoplasms of salivary gland origin which are composed of numerous and closely packed dilated acini lined with tall cuboidal or columnar cells distended with large globules of mucus, as confirmed by special stains, and presenting numerous prominent areas of well-developed squamous metaplasia, with intercellular bridges and keratinization ". Two illustrative cases of this type are described. They consider that the more malignant variants are either undifferentiated adenocarcinomata or adeno-acanthomata of salivary-gland origin. *F. W. Watkyn-Thomas*

1024. **Mixed Tumors of Salivary Gland Origin Occurring in the Palate**

J. F. GAVIN. *Archives of Otolaryngology* [*Arch. Otolaryng. (Chicago)*] **59**, 204–220, Feb., 1954. 8 figs., 15 refs.

The author describes and comments on 7 cases in which mixed tumours of salivary-gland origin occurred in the palate. Although the condition is said to be rare, all these cases were seen within a period of 4 years. In one the tumour originated in the hard palate, and in the others in the soft palate or the palatine region around the tonsil. He discusses the pathogenesis of this type of tumour and points out that although the parotid is the gland most frequently affected, the tumour may arise in any of the small salivary glands which are widely distributed in the lips, cheeks, palate, and elsewhere. According to Willis, for every 100 tumours of the parotid gland, about 10 occur in the submaxillary and 10 in the minor glands; half of these last are palatal, the least common site being the sublingual glands (about 1%). But the figures of different authorities vary greatly: Ash found 80 palatal tumours in a series of 683, and Cheyne only one in 50.

Palatal salivary tumours should be removed before they grow sufficiently large to interfere with function or cause necrosis of neighbouring tissue. In one of the author's cases there were signs suggesting metastasis to the skull; this was the only fatal case, but necropsy was not allowed. In all but one of the surviving patients the tumour was enucleated successfully, having to be removed piecemeal in the remaining case. The author advises against biopsy, pointing out that incision of the capsule for this purpose may be a cause of recurrence. *F. W. Watkyn-Thomas*

STOMACH AND DUODENUM

1025. **Treatment of Acute Gastroduodenal Haemorrhage with Particular Reference to Quantitative Blood Replacement**

F. W. GUNZ, I. D. GEBBIE, and R. C. S. DICK. *British Medical Journal* [*Brit. med. J.*] **1**, 950–956, April 24, 1954. 4 figs., 16 refs.

This paper from Christchurch Hospital, New Zealand, describes the treatment adopted in 88 cases of acute gastro-duodenal haemorrhage during the year beginning May, 1952, in which pride of place was given to the quantitative replacement of blood lost, the other therapeutic measures being dietary control, the prescription of colloidal antacids and sedatives, and, in those cases in which bleeding persisted or recurred, partial gastrectomy. In order to estimate the amount of blood lost, the plasma volume was measured by Gregersen's azovan (Evans) blue method and the total erythrocyte mass computed from the venous haematocrit reading. The " ideal " erythrocyte mass was then calculated from the patient's " ideal " weight (according to height and age), the figure of 36 ml. per kg. being taken as the normal standard. The estimated deficiency of erythrocytes was then replaced by transfusing whole blood or, if the plasma volume was large compared with the erythrocyte mass, packed cells.

The average volume of whole blood transfused was 7·9 pints (4·49 litres); this figure is among the highest reported. Emergency gastrectomy was performed in 12 cases and closure of a perforation in one, and a further 17 patients were operated on after bleeding had stopped. Among 93 admissions there were 7 deaths, giving a mortality of 7·5%, compared with 17·2% among 93 consecutive admissions for gastro-duodenal haemorrhage at the same hospital in the 18 months before the present scheme of treatment was initiated. [To the abstracter the latter figure appears to be unduly high.] The average age in the fatal cases was 65·4 years and the average age in the whole series 62·6 years.

The authors maintain that the conventional method of assessing the severity of acute blood loss and the size of

transfusion required to replace it from the clinical findings and the haemoglobin content of the peripheral blood is not sufficiently precise; in particular they point to the poor correlation between the estimated erythrocyte loss and the initial haemoglobin level in their series. They found no evidence that massive transfusion ever caused renewed bleeding, while circulatory upset due to too rapid transfusion occurred once only.

D. W. Barritt

1026. **Follow-up 3 Year Clinical Results of Combined Subtotal Gastrectomy and Subdiaphragmatic Vagotomy in 108 Cases of Duodenal (and Jejunal) Ulcer. (Comparison also of Results Obtained with Gastroduodenal and Gastrojejunal Types of Anastomosis)**
J. I. BALTZ, L. S. FALLIS, J. G. MATEER, and J. BARRON. *Gastroenterology* [*Gastroenterology*] **26**, 533–547, April, 1954. 32 refs.

In this paper the results are reported of a follow-up study of 108 out of a series of 128 patients treated at the Henry Ford Hospital, Detroit, for duodenal or jejunal ulcer by subtotal gastrectomy combined with vagotomy between 1946 and 1951, the follow-up period varying from 16 months to 3 years. Of the remaining 20 patients, 2 died postoperatively, 6 died from unrelated causes, and 12 were untraced. The results are described as "excellent" in 86·1% of the 108 cases, "fairly good" in 10·2%, and "poor" in 3·7% [but no precise definition is given of these terms]. A recurrent ulcer developed in one case only, and this responded to medical treatment. The differences in results between 68 patients who underwent a Billroth-I resection and 40 who underwent a Polya type of operation were minor and statistically insignificant. On follow-up examination after an average period of 24·5 months 88·6% [31] of 35 patients had achlorhydria to a plain test meal, and 80·0% [*sic*;=22·4] of 28 patients had achlorhydria with histamine stimulation.

[The value of this paper as a guide to the late results of surgical treatment for peptic ulcer is seriously impaired by the large proportion of cases—over 9%—that were untraced, by the shortness of the interval elapsing since operation, and by the failure to indicate clearly how many cases of duodenal and jejunal ulcer respectively were included in the original series.] *J. C. Goligher*

LIVER AND GALL-BLADDER

1027. **Blood-ammonia Levels in Relation to Hepatic Coma and the Administration of Glutamic Acid**
I. D. SINGH, J. A. BARCLAY, and W. T. COOKE. *Lancet* [*Lancet*] **1**, 1004–1007, May 15, 1954. 3 figs., 15 refs.

The authors, at the Queen Elizabeth Hospital, Birmingham, have studied the blood ammonia level in cirrhosis of the liver and the effect of giving sodium glutamate to patients with severe liver disease and hepatic coma. The blood ammonia level was higher in 12 patients with cirrhosis of the liver than in 23 healthy controls, but no correlation was found between this level and the clinical condition of the patient. The mean blood glutamine level in 10 patients with cirrhosis was slightly higher than that found in 19 controls, but the difference was not significant. Administration of large doses of sodium glutamate to 4 of the patients on 7 occasions was sometimes followed by a fall in the blood ammonia level; it did not, however, restore the level to normal. It is concluded that the high blood ammonia level in patients with cirrhosis is due to the shunting of portal venous blood away from the liver into collateral veins rather than to liver-cell damage, and that it is not in itself a cause of symptoms. *P. C. Reynell*

1028. **Esophageal Varices and Vascular Spiders (Nevi Araneosi) in Cirrhosis of the Liver**
I. B. BRICK and E. D. PALMER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 8–10, May 1, 1954. 14 refs.

The incidence of oesophageal varices and spider naevi in patients with cirrhosis of the liver was investigated by the authors at the Walter Reed Army Hospital, Washington, D.C. Oesophagoscopy was carried out on 150 patients in whom cirrhosis of the liver had been diagnosed by liver biopsy. Oesophageal varices were present in 95 patients, 59 of whom had spider naevi. Of the 55 patients without oesophageal varices, 16 had spider naevi. There was no significant difference between the two groups in the number of patients who had hepatomegaly.

The aetiology of spider naevi and their peculiar distribution—on the face, neck, chest, and arms, but rarely below the diaphragm—are discussed. In the authors' view oesophagoscopy should be carried out on all patients with spider naevi, since it is superior to *x*-ray examination for detecting the presence of oesophageal varices. *I. McLean Baird*

1029. **Alcoholism and Liver Disease.** (Alkoholism och leversjukdom)
S. MÅRTENS. *Nordisk Medicin* [*Nord. Med.*] **51**, 439–444, March 25, 1954. 34 refs.

The author does not consider that alcohol has a direct histotoxic effect on the parenchyma of the liver. At Beckomberga Hospital, Bromma, Sweden, histological examination of liver tissue obtained by needle biopsy was carried out on 32 male patients with chronic alcoholism aged 25 to 63 years. Fatty degeneration, usually confined to the centre of the lobule, was seen in 20 cases, but there was no evidence of cirrhosis in any of the specimens. There was some correlation of the fatty degeneration with the severity of the alcoholism, but not with the duration of the habit. *D. J. Bauer*

1030. **Differential Diagnosis of "Regurgitation" Jaundice: the Role of Needle Liver Biopsy**
E. R. MOVITT. *Annals of Internal Medicine* [*Ann. intern. Med.*] **40**, 932–951, May, 1954. 2 figs., 22 refs.

1031. **Fetor Hepaticus: its Clinical Significance and Attempts at Chemical Isolation**
H. R. BUTT and H. L. MASON. *Gastroenterology* [*Gastroenterology*] **26**, 829–845, June, 1954. 15 refs.

See also Chemotherapy, Abstract 969.

Cardiovascular System

1032. **Endomyocardial Fibrosis**
J. D. BALL, A. W. WILLIAMS, and J. N. P. DAVIES. *Lancet* [*Lancet*] **1**, 1049–1054, May 22, 1954. 4 figs., 21 refs.

Endomyocardial fibrosis is a common cause of heart failure in Uganda. The authors have observed it only in Africans, in whom it occurs at all ages and with equal sex incidence, and they here report 20 cases studied clinically during the period 1950–3, in all of which post-mortem proof of diagnosis was obtained. The morbid anatomical features of this condition are: normal pericardium and epicardial muscle; endocardial fibrosis in patches or involving nearly the whole of one or both ventricles, several millimetres thick, and pearly white in appearance when not concealed by thrombus; fibrosis extending up to two-thirds of the way into the myocardium; fibrosis of the papillary muscles, thickening and shortening of the chordae, and resultant incompetence of the mitral and tricuspid valves; and normal coronary arteries and aortic and pulmonary valves. Rarely, bacterial endocarditis is found.

Of the 20 patients, 14 presented with heart failure and signs of incompetence of auriculo-ventricular valves (10 mitral only, 2 tricuspid only, and 2 both mitral and tricuspid); 4 had signs and symptoms of right and left heart failure without other distinguishing features; and the remaining 2 had severe endocardial fibrosis of the right ventricle with almost complete obliteration of the inflow tract and some tricuspid incompetence—producing a clinical picture and haemodynamic upset not unlike that of constrictive pericarditis. One of these last 2 patients had a very large hydropericardium. The longest period of symptoms was 7 years and the longest period of observation 20 months. No treatment was beneficial.

[Those interested should consult this important article in the original.] *K. G. Lowe*

1033. **The Effect of Immersion Hypothermia on Coronary Blood Flow**
R. M. BERNE. *Circulation Research* [*Circulat. Res.*] 2, 236–242, May, 1954. 4 figs., 13 refs.

1034. **The Syndrome of Alternating Bradycardia and Tachycardia**
D. S. SHORT. *British Heart Journal* [*Brit. Heart J.*] **16**, 208–214, April, 1954. 3 figs., 17 refs.

In this paper from the National Heart Hospital, London, 4 cases are described in which periods of bradycardia alternated with periods of auricular tachycardia (flutter); in 3 of the 4 there was associated mitral or aortic valve disease. During the periods of bradycardia sinus arrhythmia, a wandering pacemaker, and sinus standstill were observed; the heart rate was usually between 30 and 50 per minute, increasing with exercise and emotion. During the periods of tachycardia the auricular rate varied between 180 and 300 beats per minute and the ventricular rate between 50 and 200 per minute. The symptoms were palpitation during the tachycardia, and giddiness and syncope on the cessation of tachycardia and return to the slower rhythm. In one case cerebral infarction occurred.

Treatment was difficult. The intravenous injection of atropine sulphate caused acceleration of the sinus rate in all 4 cases. Atropine by mouth (1/100 grain (0·6 mg.) thrice daily) was without effect on the heart rate. Subcutaneous injection of adrenaline caused multiple extrasystoles in one case and transient auricular fibrillation in another. The administration of ephedrine, belladonna, amphetamine, and noradrenaline by mouth were likewise unavailing. Quinidine and procainamide both caused auricular standstill with prolonged unconsciousness. Two of the patients were digitalized while in a bout of tachycardia. In one case total thyroidectomy was followed by freedom from symptoms for 18 months.

A state of subnormal activity of the sinus node is assumed to be the cause of this condition. Surgical intervention in the nervous control of the heart is judged to be hazardous and the results are considered to be unpredictable. *D. W. Barritt*

1035. **Fatal Cardiac Failure in Persons with Thoracic Deformities**
J. W. FISCHER and R. A. DOLEHIDE. *Archives of Internal Medicine* [*Arch. intern. Med.*] **93**, 687–697, May, 1954. 1 fig., 15 refs.

After briefly reviewing the literature on the subject the authors discuss the incidence of fatal heart failure occurring as a result of thoracic deformity. They were able to trace only 11 cases in which death could be attributed to this condition among 30,729 reports of necropsies performed at Cook County Hospital, Chicago—an incidence of 0·036%. Details of the 11 cases are given in a table, with case histories of 5 of them. Thoracic deformity was due to injury in 3 cases and to tuberculosis in one; in the others the cause was unknown. The clinical features were those of right heart failure, usually of short duration. All but one patient had dilatation and hypertrophy of the right side of the heart. Emphysema was found in 3 cases and bronchiectasis in 4. Pulmonary atherosclerosis was present in 7 cases.

The authors state their belief that in some cases of cardiac failure deformity of the chest may be an unrecognized aetiological factor. They point out that the physical signs may be misleading; systolic or diastolic murmurs may be present in the absence of valvular lesions. [The mechanism leading to cardiac failure in these cases is not clearly indicated.]

[The fact that the 5 patients mentioned in detail all died shortly after the administration of morphine once again emphasizes the danger of that drug in this type of cardio-respiratory failure.] *F. Starer*

DIAGNOSTIC METHODS

1036. **Intracardiac Phonocardiography**
K. YAMAKAWA, Y. SHIONOYA, K. KITAMURA, T. NAGAI, T. YAMAMOTO, and S. OHTA. *American Heart Journal* [*Amer. Heart J.*] **47**, 424–431, March, 1954. 9 figs., 5 refs.

The sound waves originating in the heart which are recorded by the phonocardiograph from the chest wall must have been damped and distorted by their passage through the thorax. In order to record the sounds from within the heart the authors, working at Tokyo University School of Medicine, have devised a capacitor microphone consisting of a small insulated metal stick fixed to the tip of a plastic catheter and connected to the grid of the oscillator circuit by a fine screened wire, the frequency of the carrier wave being 480 kc.p.s. It was assumed that, on passing the catheter into the heart, the dielectric change caused at its tip by the vibrations which are the reputed cause of the heart sounds could thus be transmitted by frequency modulation to an oscillograph and converted into sound through a loud-speaker. Under fluoroscopic control the catheter microphone was introduced into the left or right heart in more than 20 experiments on dogs, and into the right heart in 3 human subjects, in one of whom it reached the pulmonary artery.

Several of the phonocardiograms obtained are reproduced and described, and record murmurs which are not present in synchronous chest-wall recordings. Different patterns were obtained according to whether the catheter was free in the blood stream or touching the heart wall, the latter corresponding more closely to those of chest-wall recordings.

The results obtained suggest that there is whirlpooling within the heart and arteries, the vibrations of which are inaudible through the chest wall owing to the damping effect of the heart and arterial walls, and that the heart sounds as normally heard are chiefly due to the vibration of solid structures. *D. Goldman*

1037. **The Role of Auscultation in the Diagnosis of Congenital Heart Disease. A Phonocardiographic Study of Children**
J. D. L. REINHOLD and A. S. NADAS. *American Heart Journal* [*Amer. Heart J.*] **47**, 405–423, March, 1954. 17 figs., 14 refs.

The auscultatory signs of congenital heart disease were studied in 64 children aged 5 to 15 years at the Children's Medical Center (Harvard Medical School), Boston. Particular attention was paid to phonocardiograms, which were recorded with stethoscopic and logarithmic microphones from the apex, second and fourth left intercostal spaces, and the second right intercostal space parasternally. A detailed description of the normal phonocardiogram is given, and the authors then recount their findings in cases of aortic stenosis, pulmonary valvular stenosis, ventricular and atrial septal defect, Fallot's tetralogy, and atypical patent ductus arteriosus. Illustrative phonocardiograms and composite diagrams showing the time-relations of the various features with those of the electrocardiogram, apex cardiogram, and carotid pulse tracing are presented, and reference is made to the intensity, distribution, and transmission of the sounds and murmurs described.

The study revealed several rather characteristic phonocardiographic appearances. Among the more valuable points of differential diagnosis was the degree of splitting of the second heart sound, which was greatest with atrial septal defects, normal (0·04 second or less) in cases of ventricular septal defect or patent ductus arteriosus, and negligible in pulmonary and aortic stenosis. In normal children, the second sound is louder on the left than on the right side in the second intercostal space. This relationship is preserved in the majority of cases of atrial septal defect, small ventricular septal defects, and patent ductus arteriosus, but is usually exaggerated in the presence of pulmonary hypertension and reversed in cases of pulmonary stenosis. The tracing of the systolic murmur of aortic stenosis was best obtained from the second right space and was of a characteristic diamond configuration, rising to a peak at the end of the first third of systole, whereas a late crescendo systolic murmur, best recorded from the second left space, characterized a patent ductus arteriosus. Plateau or decrescendo systolic murmurs were registered in cases of septal defect.

The authors state their belief that a search for these phenomena, and others which they describe, by auscultation and their occasional registration by phonocardiography may help in the differential diagnosis of congenital heart disease. *D. Goldman*

CHRONIC VALVULAR DISEASE

1038. **Tricuspid Incompetence**
O. MÜLLER and J. SHILLINGFORD. *British Heart Journal* [*Brit. Heart J.*] **16**, 195–207, April, 1954. 14 figs., 21 refs.

In view of the varied opinions expressed regarding the incidence and the diagnostic criteria of tricuspid incompetence, the authors, working at Hammersmith Hospital (Postgraduate Medical School of London), have investigated 21 cases of this condition by means of pressure recordings from the right heart, venous pulse tracings, and phonocardiography. Rheumatic heart disease with mitral stenosis was present in 13 of the cases. All the patients complained of dyspnoea, but this was usually not severe and in one case the dyspnoea diminished as tricuspid incompetence developed. In all cases the venous pressure was raised, often greatly, and in 16 pulsation of the usually enlarged liver accompanied pulsation of the neck veins. An icteric tinge was noted in 4 cases, auricular fibrillation in 17 cases, and sinus rhythm in 4 cases.

The earliest clinical sign of tricuspid incompetence was a systolic murmur which was loudest in the 4th left interspace close to the sternum and tended to be transmitted well to the epigastrium. The intensity of the murmur was increased by exercise and by inspiration, and also marked after a long diastolic pause when the rhythm was irregular; phlebograms showed that this was

directly due to an increase in the degree of tricuspid incompetence. In 9 cases a short, low-pitched, early diastolic murmur was heard; in one of these cases subsequent necropsy showed only dilatation of the valve ring. In the presence of concomitant mitral valve disease the murmurs of tricuspid incompetence were distinctive in 8 cases, but could not be distinguished with certainty from the apical murmurs in the remaining 5.

Jugular phlebograms were obtained in all the cases. Modification of the jugular venous pulse took the form of incomplete or complete obliteration of the systolic negative x wave by a positive systolic wave. In all 12 cases in which intracardiac pressures were recorded there was a rise in the right auricular pressure, the auricular pressure tracings showing a positive systolic wave the height of which varied with the degree of incompetence. Differential pressure records between the right auricle and superior vena cava showed a reverse flow from the right auricle to the superior vena cava throughout systole. The electrocardiographic patterns were determined by the type of heart disease and not by the tricuspid lesion. Radiological examination of the contour and movements of the heart gave disappointing results. In the 4 cases which came to necropsy no gross distortion of the tricuspid valve cusps was found.

The authors conclude that some degree of tricuspid incompetence is extremely common in all forms of cardiac failure. The earliest clinical sign is the systolic murmur, followed by a systolic wave in the jugular venous pulse and an expansile liver. Organic lesions of the tricuspid valve are relatively rare and cannot be distinguished by clinical or instrumental methods from the more common functional tricuspid incompetence. *D. W. Barritt*

1039. **Assisted Circulation by Pump-oxygenator during Operative Dilatation of the Aortic Valve in Man**
I. Aird, D. G. Melrose, W. P. Cleland, and R. B. Lynn. *British Medical Journal* [*Brit. med. J.*] **1**, 1284–1287, June 5, 1954. 8 refs.

The authors briefly discuss the literature relating to the clinical application of extracorporeal circulation by means of an artificial heart–lung machine. One of the main risks of cardiac surgery is the danger of inadequate coronary flow, which may result in the development of ventricular fibrillation. An apparatus, consisting essentially of a pump–oxygenator, has been devised and described by Melrose *et al.* (*Brit. med. J.*, 1953, **2**, 57 and 62; *Abstracts of World Medicine*, 1954, **15**, 139) whereby the circulation may be assisted and which may therefore prevent the onset of fibrillation by maintaining an efficient coronary circulation.

In the present paper from the Postgraduate Medical School of London a full description is given of a case of mitral incompetence with aortic stenosis in which this apparatus was used and double cardiotomy successfully performed. The patient, a woman aged 32, had been previously considered too bad an anaesthetic risk to justify even the operation of appendicectomy. Blood was removed from the inferior vena cava by a catheter inserted in the saphenous vein, passed through the machine, and then returned to the aorta by way of a catheter in the superficial femoral artery. The operation lasted for some 2½ hours, during which the patient lost 6 pints (3·4 litres) of blood, for which a transfusion of 7½ pints (4·3 litres) was given. The mixed venous blood in the machine during operation showed an oxygen saturation of 76 to 78% and a carbon dioxide content of 45 to 47 volumes %. The flow of blood in the machine varied from 500 to 800 ml. per minute, and it was estimated that in all some 70 litres of blood passed through the pump–oxygenator, or about 30% of the total cardiac output. Recovery was uneventful apart from some cyanosis, which passed off within 4 hours, and thrombophlebitis of the catheterized saphenous vein, and the patient's condition has been greatly ameliorated. The authors feel that this case shows that the use of the apparatus in man is safe and hope that with increasing experience it will be possible in future to take over a larger part of the circulation. *J. R. Belcher*

1040. **Aortic Stenosis. Diagnosis and Treatment**
A. Logan and R. Turner. *Lancet* [*Lancet*] **1**, 1091–1095, May 29, 1954. 7 figs., 5 refs.

In reporting 9 cases of aortic stenosis treated by aortic valvotomy at the Western General Hospital, Edinburgh, the authors review the symptoms and clinical signs of the disease, together with the radiological, electrocardiographic, and phonocardiographic features. They suggest that the diagnosis in such cases is often missed because even severe stenosis may exist in the absence of some of the classic signs.

The operation consisted in dilatation of the aortic valve, approached by the ventricular route, by means of a mechanical dilator similar in type to the Brock pulmonary dilator but larger in size, the blades being 10 cm. long and the maximum spread 4 cm. Of the 9 patients operated on, 4 had associated mitral disease, and in these the two valvotomies were performed at the same thoracotomy, the aortic valve being dealt with before the mitral valve. Several illustrative case histories are given.

Only one of the 9 patients died as a result of the operation, the condition of all the rest being improved. Even so the authors point out that these patients were all in an advanced stage of the disease, and the benefit obtained might have been still greater had they been treated earlier. They admit the difficulty of assessing the degree of stenosis, but are of the opinion that patients with evidence of increasing left ventricular hypertrophy should be subjected to operation even in the absence of symptoms.
J. R. Belcher

1041. **Commissurotomy for Rheumatic Aortic Stenosis. I. Surgery**
C. P. Bailey, H. E. Bolton, W. L. Jamison, and H. T. Nichols. *Circulation* [*Circulation* (*N.Y.*)] **9**, 22–31, Jan., 1954. 12 figs., 11 refs.

Although a number of workers have contended that aortic stenosis is arteriosclerotic in origin, the present authors believe that it is usually the result of rheumatic infection, the commissures between the valve cusps becoming united as a result of the rheumatic process. If the condition is associated with a mitral lesion known

to be rheumatic, then the probability of the aortic lesion being also of rheumatic origin is very high. The malformation present in the case of congenital aortic stenosis is of a different type and requires different surgical treatment.

At the Hahnemann Medical College and Hospital, Philadelphia, the authors have attempted to treat aortic stenosis by using a triradiate dilator (illustrated) which engages and ruptures the commissures. Of 27 patients with pure aortic stenosis so treated, 6 (22%) died, probably because some of the cases were really congenital in origin and the valve had only two cusps, while in others because the heart muscle was unduly soft. On the other hand, of 35 with combined aortic and mitral lesions, 5 died, a mortality of only 14%, this lower figure being attributed to the smaller size of the left ventricle, which was less irritable than in the other forms.

In consequence of the dangers and difficulties associated with the transventricular approach and of the considerable discrepancy in mortality between the two groups described above, the authors have devised and carried out a retrograde approach through the wall of the ascending aorta. A pouch, which is formed by suturing a flap of pericardium to the edges of the incision into the aorta, controls bleeding and permits introduction of the valvotome. More recently a plastic pouch has been used to help in this procedure. This transaortic operation seems to be well tolerated, but the number of cases treated so far is still too small for definite conclusions to be drawn. The operation is not suitable for elderly patients, in whom the aortic wall may be friable.

T. Holmes Sellors

1042. **Surgical Treatment of Mitral and Aortic Stenoses. Results of One Hundred Fifteen Valvotomies**

D. A. COOLEY and M. E. DEBAKEY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 235–239, May 15, 1954. 1 fig., 18 refs.

The operative fatality rate in the 110 patients undergoing mitral valvotomy was 9%. Death was due to thrombosis and embolism in 9 of these 10 patients. Good to excellent functional results were obtained in 74% of the survivors, in many of whom normal activity was resumed and heart murmurs completely disappeared. Results were more uniformly good in patients between the ages of 25 and 35 years, although striking improvement was noted in many of the severely incapacitated persons in the older age group.

Factors such as history of embolism, auricular fibrillation, valval calcification, and associated valval lesions should not be considered contraindications to valvotomy, although they admittedly increase the surgical risk. Mitral commissurotomy can be successfully performed on pregnant women with subsequent normal delivery. This was accomplished in 5 patients in the series reported. Commissurotomy should preferably be performed before the fifth month of pregnancy. Recurrence of severe stenosis after successful valvotomy is rare and was not noted in any of our patients.

Aortic stenosis presents a more complex therapeutic problem, but symptoms of reduced cardiac output have been relieved by valvotomy in properly selected cases. Aortic valvotomy was performed on 3 patients with acquired and 2 with congenital aortic stenosis. Two critically ill patients with the former type died; the other patient in this group was improved by operation. Valvotomy considerably relieved the symptoms in both patients with congenital aortic stenosis. It is important to perform aortic valvotomy before the cardiac enlargement becomes pronounced and accompanying coronary insufficiency develops.—[Authors' summary.]

1043. **A Method for the Surgical Correction of Mitral Insufficiency. I. Preliminary Considerations**

J. C. DAVILA, W. W. MATTSON, T. J. E. O'NEILL, and R. P. GLOVER. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **98**, 407–412, April, 1954. 5 figs., 10 refs.

The loss of valve substance in mitral regurgitation may be absolute or relative. In the latter case the reflux is increased owing to enlargement of the auriculo-ventricular ring as a result of dilatation and hypertrophy of the left heart. Various methods of surgical treatment have been attempted from time to time without marked success. Slings or flaps placed below the valve have been used, and invagination of the auricular appendix through the orifice so as to narrow and buttress it. Suture of the valve cusps themselves has been suggested as another method.

The present authors discuss the feasibility of narrowing the mitral ring by means of a purse-string suture so as to reduce the size of the orifice. The anatomy and relations of the ring are described in detail, and the varying positions of the coronary arteries and cardiac veins in relation to the ring are discussed.

T. Holmes Sellors

1044. **Physiopathological Concepts of Mitral Valvular Disease. Review of 225 Cardiotomies**

J. STORER, P. LISAN, J. E. DELMONICO, and C. P. BAILEY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 103–106, May 8, 1954. 3 figs., 3 refs.

The study here reported from Hahnemann Medical College and Hospital, Philadelphia, was primarily designed to investigate the problem of atrial thrombosis and was based on 225 surgically treated cases of mitral valvular disease not complicated by lesions of the other valves. They were divisible into 3 groups, each of 75 cases, as follows: (I) " pure " mitral stenosis; (II) mixed lesions, predominantly stenotic but with some regurgitation; and (III) " pure " mitral incompetence.

The following observations were made. (1) The clinical diagnosis of the exact mitral lesion before operation was in error in 27% of cases in Group I, in 38% in Group II, and in 65% in Group III, these figures showing that the addition of mitral insufficiency made accurate diagnosis more difficult. (2) The average age of patients in Group III was significantly lower than that of those in Group I or II, indicating that incompetence is probably a more incapacitating lesion than stenosis. (3) The ratio of females to males was 3:1 in Groups I and III, but the numbers were nearly equal in Group II. (4) A higher

incidence of fibrillation in Group III was thought to be due to the greater atrial dilatation seen in these cases. (5) Intracardiac thrombosis occurred in 44% of cases in Group I, in 18·6% in Group II, and in 9·1% in Group III. It is suggested that the disturbance in the atrial blood produced by the jet of blood in incompetence reduces the chances of clot formation. (6) Three conditions of the valve were distinguished: (*a*) flexible (26% of the whole series), (*b*) thickened (33%), and (*c*) calcified (41%). Calcification was notably high in Group II (76% of cases, compared with 28% in Group I and 18·6% in Group III). It is thought that the presence of calcification in such a high percentage of cases in Group II was partially responsible for the accompanying incompetence.

The authors conclude that stenosis and auricular fibrillation predispose to atrial thrombosis, whereas incompetence decreases this risk, and that the presence of calcification in a stenotic valve increases the likelihood of incompetence. *W. P. Cleland*

CONGENITAL HEART DISEASE

1045. **Cessation of Circulation in General Hypothermia. III. Technics of Intracardiac Surgery under Direct Vision**
H. SWAN and I. ZEAVIN. *Annals of Surgery* [*Ann. Surg.*] **139**, 385–396, April, 1954. 5 figs., bibliography.

In experimental animals occlusion of the inflow to the heart for the purposes of intracardiac surgery under direct vision can be maintained safely at normal temperatures for 1½ minutes, and with only slight risk up to 4 minutes. Thereafter the mortality rises sharply, death being due to ventricular fibrillation or cerebral changes.

The use of hypothermia during cardiac operations in man, as pioneered by Bigelow, enables the great veins to be occluded for periods up to 15 minutes, while the danger of ventricular fibrillation can be obviated to some extent by hyperventilation and infusion of potassium salts. The authors have operated on 16 patients under hypothermia at the University of Colorado School of Medicine, Denver, with 2 deaths. The process of cooling, which is carried out under general anaesthesia in a bath of ice water at 2° to 4° C., may take anything from 15 minutes to 1¼ hours. It is noted that fat persons cool more slowly than thin. The operation is carried out when the temperature is between 23° and 26° C. For repair of an interatrial septal defect the authors divide the sternum transversely, ligate the azygos vein, and then occlude the venae cavae by means of check ligatures. After 45 seconds to allow the heart to empty, the root of the aorta is clamped at the level of the coronary arteries. Temporary tourniquets are placed around both lung roots to control the inflow from the pulmonary circulation. When the repair has been effected the chest is filled with saline before the wound in the heart is clamped and the circulation restored; in this way the danger of air embolism is avoided. The authors obtained good results in 4 out of 5 patients treated in this way.

The major complication is ventricular fibrillation, for the treatment of which the authors have found little value in electrical defibrillation and prefer to perfuse the coronary arteries with potassium chloride solution (1 mEq. per litre) followed by cardiac massage, which is maintained as the patient is warmed. Some hearts recover as the temperature rises; the use of adrenaline is not recommended. *T. Holmes Sellors*

1046. **Coarctation of the Pulmonary Artery**
T. SØNDERGAARD. *Danish Medical Bulletin* [*Dan. med. Bull.*] **1**, 46–48, April, 1954. 4 figs., 3 refs.

The author describes 3 cases of cyanotic congenital heart disease in which at operation (in one case at the Rigshospital, Copenhagen, and in 2 at the Kommunehospital, Aarhus) the pulmonary artery was found to be constricted at its bifurcation. This condition, for which the term "coarctation of the pulmonary artery" is suggested, does not seem to have been previously suspected. In all 3 cases the constriction involved the first part of each branch of the pulmonary artery, and fibrous bands from the ligamentum arteriosum appeared to take part in the constriction.

The author states that coarctation of the pulmonary artery is more serious than that of the aorta, because in the former it is not possible to establish a collateral circulation as in the case of the aorta. He considers that the condition can be recognized only if the pericardium is opened in all operations on patients in whom it might be suspected to occur. *G. S. Crockett*

1047. **Further Observations on the Closure of Atrial Septal Defects**
H. B. SHUMACKER, H. KING, and P. R. LURIE. *Circulation* [*Circulation (N.Y.)*] **9**, 504–510, April, 1954. 4 figs., 10 refs.

In an earlier paper (*Amer. Surg.*, 1953, **138**, 404) a new technique for closure of an atrial septal defect was described in which a half-moon-shaped pocket of pericardium was sutured to an incision in the atrial wall, this pocket being then invaginated into the atrial cavity so that its posterior wall could be sutured to the wall of the septal defect. This procedure, although satisfactory in dogs, was not successful in 2 patients, one of whom died 5 months after operation; at necropsy it was found that the graft had completely disappeared, this being attributed to failure of revascularization of the pericardium. In the present paper from Indiana University School of Medicine, Indianapolis, the authors describe a modification of this method in which thin, finely-woven nylon fabric was used instead of pericardium. By this technique a large septal defect which had been produced experimentally in 13 dogs was closed. The animals were killed 11 to 189 days after operation and necropsy showed complete closure in 12; in the remaining animal there was a defect 1 mm. in diameter. In 2 dogs the graft was not covered by endothelium 11 and 19 days respectively after operation. No gross thrombi were visible in the atrium or on the graft, and in no instance was there obstruction to the venae cavae or coronary sinus.

This operation was performed with success on a boy aged 11 years with an atrial septal defect about 2 cm.

in diameter and pulmonary stenosis. The septal defect was closed by invaginating the nylon pocket into the atrium and fixing it to the edge of the septal defect with four interrupted sutures of 4-0 silk and four continuous sutures of the same material between the interrupted sutures. A pulmonary valvotomy was also performed. The patient was well and free from symptoms 5½ months after operation. *R. L. Hurt*

1048. **Tuberculosis and Congenital Cyanotic Heart Disease**

R. D. SLOAN, C. R. HANLON, and H. W. SCOTT. *American Journal of Medicine* [*Amer. J. Med.*] **16**, 528–534, April, 1954. 3 figs., 13 refs.

The chest radiographs of 800 patients with congenital pulmonary stenosis who were subjected to thoracotomy at the Johns Hopkins Hospital, Baltimore, were examined to ascertain the incidence of pulmonary tuberculosis in such patients.

The criteria for the diagnosis of primary or re-infection tuberculosis are discussed. While admitting that estimates from such an investigation can be misleading, the authors believe that the maximum possible incidence of pulmonary tuberculosis in congenital cyanotic heart disease is less than 2%. About 75% of the patients were under 10 years of age; the incidence of tuberculosis was highest (two-thirds of the cases) in the remaining 25%.

Reasons are given for the view that a tuberculous focus may be reactivated if the lung is perfused with systemic arterial blood. Discussion is therefore centred on the possible means of avoiding this when planning an operation for the relief of pulmonary stenosis in the presence of pulmonary tuberculosis. The authors suggest three suitable operative procedures: an end-to-end subclavian–pulmonary anastomosis on the side opposite to the diseased lung; pulmonary valvotomy; or an anastomosis on the side of major tuberculous involvement followed by resection of an appropriate amount of diseased lung tissue. Two cases are described in which the first and third of these were carried out respectively; in the first case the lung lesion remained stable for 2 years after the anastomosis but eventually broke down and lobectomy proved fatal; in the second, a case of Fallot's tetralogy, the patient did not survive operation.

R. S. Stevens

CORONARY DISEASE AND MYOCARDIAL INFARCTION

1049. **Peripheral Arterial Embolism after Myocardial Infarction. Occurrence in Unsuspected Cases and Ambulatory Patients**

B. G. LARY and G. DE TAKATS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 10–13, May 1, 1954. 19 refs.

The authors examined the case records at St. Luke's Hospital, Chicago, for the period 1938 to 1950 to determine the incidence of peripheral arterial embolism after myocardial infarction. It was found that out of a total of 27 cases of arterial embolism of the limbs from all causes, myocardial infarction preceded the arterial embolism in 7.

Analysis of these 7 cases and a further case seen in 1953 established that the common denominator was inadequate rest in bed. It was also noted that none of the patients had received anticoagulant therapy. The mortality in such cases is high; 6 of the 8 patients in this series died. The authors admit that "such a small series of cases is not statistically significant", but suggest that too little attention has been paid to early ambulation as a factor in the causation of embolic phenomena. Patients with coronary infarction who come under their care are given anticoagulants and kept at rest in bed for at least 6 weeks. *I. McLean Baird*

1050. **The Treatment of Shock Associated with Myocardial Infarction**

G. C. GRIFFITH, W. B. WALLACE, B. COCHRAN, W. E. NERLICH, and W. G. FRASHER. *Circulation* [*Circulation (N.Y.)*] **9**, 527–532, April, 1954. 13 refs.

For the purposes of this investigation, carried out at Los Angeles County Hospital, of the effect of the shock which is associated with myocardial infarction, a systolic blood-pressure reading of 80 mm. Hg or below in previously normotensive patients, or of 100 mm. Hg or below in formerly hypertensive patients, was accepted as evidence of shock, provided the hypotension lasted for an hour or more and was accompanied by signs of peripheral circulatory collapse. Examination of the records of 816 cases of myocardial infarction admitted during 18 months in 1949–51 showed that of these patients 161 (20%) had evidence of shock as defined and 128 of these died, a mortality of 81%.

The later group now described consisted of 134 patients with shock due to recent myocardial infarction who were admitted to the hospital during 18 months in 1951–2. The importance of early treatment of shock is emphasized by the fact that of the 60 patients treated within 3 hours of onset only 8 died, a mortality of 13%, compared with 56 (76%) of the 74 patients treated after 3 hours; the over-all mortality in the whole group was 47·8%.

If routine treatment did not control shock, one or more of the following additional measures were employed. Intravenous infusion (9 cases, control of shock in 2); retrograde arterial infusion of plasma or blood into the radial artery (19 cases, shock controlled in 12); administration of noradrenaline by intravenous drip using a solution of 8 mg. in 1 litre of 5% glucose in water (30 cases, shock controlled in 17); methoxamine, given either intramuscularly in a dose of 20 mg., or 5 mg. slowly intravenously and repeated as necessary (49 cases, shock controlled in 10, no pressor effect obtained in 35); *iso*propylnoradrenaline, 2 to 3 mg. slowly intravenously, followed by 7·5 or 15 mg. sublingually as required after shock had been overcome, given at intervals of 15 or 30 minutes (26 patients, shock controlled in 7, no pressor effect in 16). The administration of ACTH (corticotrophin), cortisone, or cholinesterase to several selected patients had no noticeable beneficial effect.

A. Schott

1051. **Immediate Hemodynamic Effects of Acute Coronary Artery Occlusion**
R. WÉGRIA, C. W. FRANK, G. A. MISRAHY, H. WANG, R. MILLER, and R. B. CASE. *American Journal of Physiology* [*Amer. J. Physiol.*] **177**, 123–127, April, 1954. 1 fig., 9 refs.

In experiments at the Columbia University College of Physicians and Surgeons and the Presbyterian Hospital, New York, myocardial infarction was produced by coronary ligation in dogs under chloralose anaesthesia and the haemodynamic effects noted. It was found that the cardiac output and arterial pressure fell together at first and then rose again. When the blood pressure was reduced it was always due to a decrease in cardiac output. [Such acute experiments do not throw light on the *progressive* fall in blood pressure observed over several days after a clinical infarction.] *J. McMichael*

PERIPHERAL ARTERIES

1052. **The Incidence and Severity of Atherosclerosis in Estrogen-treated Males, and in Females with a Hypoestrogenic or a Hyperestrogenic State**
A. U. RIVIN and S. P. DIMITROFF. *Circulation* [*Circulation (N.Y.)*] **9**, 533–539, April, 1954. 1 fig., 28 refs.

In order to explore the possibility that oestrogenic hormones may inhibit the development of atherosclerosis, a study was made of the necropsy records of male patients with carcinoma of the prostate who had been treated with oestrogens and of female patients with carcinoma of the breast—these two groups being considered to have been in a state of hyperoestrogenism—and of surgically castrated females, who had thus been in a state of hypooestrogenism. The degree of atherosclerosis present at necropsy in the coronary arteries, aorta, and cerebral arteries in each case was recorded as: (1) minimal or none, or (2) moderate or severe. The findings in each group were compared with those in similar groups of subjects whose oestrogen supply had been normal. Cases of diseases causing hypercholesteraemia were discarded, but cases of hypertension were included. Cachexia does not appear to affect the incidence of atherosclerosis, and cachectic subjects were therefore not excluded.

In all, 153 cases of carcinoma of the prostate were studied. These were divided into cases treated with oestrogens for 3 months or more and control cases in which less than 3 months' oestrogen treatment or none at all had been given. The treated cases were further subdivided according to the dosage employed: (*a*) 30 cases in which a dose of 75 mg. of stilboestrol or more had been given daily, which were compared with 27 controls, a significant difference in severity of atherosclerosis being found only in the coronary arteries; (*b*) 23 cases in which an average dose of 5 mg. of stilboestrol daily had been given, which were compared with 73 controls, no significant difference being found in the severity of the atherosclerosis present at any site. On the other hand the incidence of atherosclerosis in 39 cases of carcinoma of the breast was lower than that in a series of normal subjects reported by other workers, while that in 99 female subjects who had undergone bilateral oophorectomy at least one year before death and before the age of 50 was significantly higher.

These results are held to support the theory that ovarian secretions protect against atherosclerosis, this accounting for the sex difference in incidence of the disease. *Peter Harvey*

HYPERTENSION

1053. **Hypotensive Action of Reserpin**
A. E. DOYLE and F. H. SMIRK. *Lancet* [*Lancet*] **1**, 1096–1097, May 29, 1954. 7 refs.

To determine whether reserpine, an alkaloid of *Rauwolfia serpentina*, acts as a placebo or a sedative or has a definite hypotensive effect, large doses were given to 20 hypertensive patients at the University of Otago Medical School, Dunedin. The dose of reserpine usually given is 0·75 to 1·5 mg. daily, but in this investigation it was decided to try the effect of 2 to 3 mg. by mouth three times a day. After these large doses the blood pressure usually fell significantly, more so than after a placebo, the trough occurring 5 hours after the dose. For example, the systolic pressure fell more than 40 mm. Hg in 16 patients and more than 60 mm. Hg in 12, while the diastolic pressure fell more than 25 mm. Hg in 17 patients and more than 45 mm. Hg in 7. The fall in blood pressure began on the first or second day of treatment and often persisted for 24 hours after treatment ceased. There were, however, unpleasant side-effects with these large doses, including flushing, conjunctival injection, nasal blockage, fatigue and sleepiness, depression, shivering, restlessness, and a sensation of heat. Postural hypotension was much less marked than that observed after administration of methonium compounds; nevertheless patients preferred hexamethonium, even though this was given by injection. Small doses of reserpine did not induce an adequate fall in blood pressure. In some cases reserpine given with hexamethonium had an additive effect; it is suggested that this may prove a useful combination. *Arthur Willcox*

1054. **Arterial Hypertension Treated with *Rauwolfia serpentina* and *Veratrum viride***
C. JOINER and R. KAUNTZE. *Lancet* [*Lancet*] **1**, 1097–1099, May 29, 1954. 10 refs.

A clinical trial was conducted at Guy's Hospital, London, in which hypertensive patients taking veratrum viride in the form of "veriloid" were also given rauwolfia serpentina. This treatment was suggested by reports that rauwolfia possessed additive properties in lowering the blood pressure when given with other hypotensive drugs. A total of 24 patients were selected for the trial, but 8 had to be withdrawn before the end; thus the results in 16 cases only are presented. All the patients received veriloid, 1 mg. per 10 lb. (4·5 kg.) body weight, throughout the 16 weeks of the trial. Rauwolfia was given in addition to the veriloid—to 10 patients in a nightly dose of 0·5 g. for the second 8 weeks of the study,

and to 6 patients in a nightly dose of 0·5 g. for the first 8 weeks and of 1 g. for the remaining 8 weeks.

The addition of rauwolfia serpentina resulted in a bradycardia in 6 patients; in 6 others there was a fall in diastolic pressure, which was, however, clinically significant only in 3 (a fall of 14 to 45 mm. Hg). Increasing the dose of rauwolfia from 0·5 to 1 g. had no effect in the 6 cases in which this was done. No serious toxic effects were observed, but in 2 patients pruritus with urticaria developed.

The authors conclude that in the dosages used there is no clear evidence of an additive effect of the two drugs.

Arthur Willcox

1055. **A Clinical Appraisal of Pentapyrrolidinium (M & B 2050) in Hypertensive Patients**

E. D. Freis, E. A. Partenope, L. S. Lilienfield, and J. C. Rose. *Circulation* [*Circulation* (*N.Y.*)] **9**, 540–546, April, 1954. 8 refs.

The authors report, from Georgetown University and the Veterans Administration Hospital, Washington, D.C., the results of a comparative study of the effect of a new ganglionic blocking agent, pentamethylene 1:5-bis-(1-methylpyrrolidinium) bitartrate (pentapyrrolidinium, " M and B 2050 ") and hexamethonium chloride on the blood pressure of hypertensive patients. In acute experiments on 4 patients to whom intravenous injections of the two drugs were given (at several days' interval) sufficient to produce a significant and equal reduction in arterial pressure, pentapyrrolidine was found to be about five times more potent than hexamethonium and the duration of its effect 40% longer. In 27 patients with severe fixed hypertension treated during 2 to 6 months solely with pentapyrrolidine given orally in three doses a day, the mean total daily effective dose was 300 mg. (range 135 to 630 mg.). In these patients the average blood pressure fell from 230/135 mm. Hg (range 180/110 mm. to 260/160 mm. Hg) before treatment to 170/110 mm. (range 130/95 to 210/130 mm. Hg) after treatment.

Cross-tolerance between the two drugs was very small, and tolerance developed to pentapyrrolidine less often than to hexamethonium. Ingestion of alcohol or of a large meal, vigorous exercise, hot weather, salt depletion, and diuresis induced by mercurials intensified the hypotensive effect of pentapyrrolidine. The drug when given orally also produced less constipation than hexamethonium, and this could be controlled by administration of neostigmine or of aperients; with parenteral administration constipation did not occur. The other side-effects of the drug were similar to those of hexamethonium, impotence being particularly frequent and troublesome. One important advantage of pentapyrrolidine was that its onset of action was far more predictable than that of hexamethonium and, in contrast to the latter, oral administration lowered the blood pressure significantly without producing prolonged collapse or paralytic ileus. It is emphasized, however, that critical adjustment of the dose is necessary, which is a definite drawback, since a slight excess may produce hypotensive reactions such as postural faintness, and slight underdosage may fail to lower the blood pressure significantly. The authors therefore recommend that its use be confined to cases of severe hypertension which have not been benefited by simpler measures. *A. Schott*

1056. **Further Evaluation of Hydralazine in Treatment of Hypertensive Disease**

R. D. Taylor, A. C. Corcoran, H. P. Dustan, and I. H. Page. *Archives of Internal Medicine* [*Arch. intern. Med.*] **93**, 705–712, May, 1954. 15 refs.

Opinion on the value of hydrallazine (1-hydrazinophthalazine) in the treatment of hypertension is still divided. The authors report the results of giving this drug to 86 out-patients at the Cleveland Clinic Foundation, Ohio. [This is a follow-up of a series previously reported (*Arch. intern. Med.*, 1952, **90**, 734; *Abstracts of World Medicine*, 1953, **14**, 43).] The dose used was 25 mg. increasing to 200 mg. four times a day. Patients were classified into two groups, those whose diastolic pressure fell persistently below 110 mm. Hg being regarded as " responders ". There were 54 patients in this group; 5, however, later became unresponsive. It was possible to follow up 43 " responders " for a total of 30 months. These were compared with 32 patients from the earlier series who had shown no response. The severity of the hypertension before treatment was started was comparable in the two series.

During the period of study 3 " responders " (7%) and 11 " non-responders " (34%) died. While diastolic pressure was always reduced in " responders ", systolic pressure remained elevated and labile; the severity of retinopathy, proteinuria, and haematuria was also reduced. Some of these patients no longer required salt restriction to prevent congestive failure. No similar improvement occurred amongst " non-responders ".

Hypertension of neurogenic origin showed the greatest improvement, while none of 5 patients with renal hypertension derived any benefit. On the other hand, 9 out of 13 patients with malignant hypertension did well.

The authors state that 50% of a given group of hypertensives may be expected to show a sustained response to hydrallazine treatment, the main criterion being reduction in diastolic pressure. Isolated readings may, however, be misleading. Side-effects are frequent but usually transitory, and include flushing, headache, and tachycardia. They can be controlled by antipyretics and antihistamines. Frequently the effect of the treatment is not seen for several weeks. Its use is not indicated in early hypertension or in rapidly advancing malignant hypertension. The drug probably acts on a central nervous regulatory mechanism.

It is concluded that hydrallazine is of definite value in the treatment of certain types of hypertension.

[For details of the method of grading used and of the dosage schedule the earlier publication should be consulted.] *F. Starer*

1057. **Pilocarpine as an Antagonist to the Undesired Effects of Ganglion-blocking Agents in the Treatment of Hypertension**

J. A. Gunn and A. M. Cooke. *British Medical Journal* [*Brit. med. J.*] **1**, 1473, June 26, 1954. 1 ref.

Haematology

1058. **Immunoleucopenia and Immuno-agranulocytosis.** (Immuno-Leukopenien und Immuno-Agranulozytosen)
S. MOESCHLIN. *Annales paediatrici* [*Ann. paediat. (Basel)*] **182**, 255–270, May, 1954. 10 figs., 13 refs.

Previous observations having shown that amidopyrine agranulocytosis is mediated through the production of leucocyte agglutinins (Moeschlin and Wagner, *Acta haemat. (Basel)*, 1952, **8**, 29; *Abstracts of World Medicine*, 1952, **12**, 56), the author now describes a case of primary atypical pneumonia in which the blood serum contained a cold agglutinin of high thermal amplitude (that is, it was still active above room temperature), and in which there was an acute haemolytic anaemia and a chronic granulocytopenia and thrombocytopenia due to the presence of leucocyte agglutinins. He has also found similar agglutinins in one case of agranulocytosis due to sulphapyridine, 3 of lupus erythematosus disseminatus, one of infectious mononucleosis, one of rheumatoid arthritis, and one of myelomatosis with hyperglobulinaemia, and suggests that all such cases should be regarded as examples of "immunoleucopenia" or "immuno-agranulocytosis", a type distinct from the granulocytopenias due to marrow obliteration (as by osteosclerosis), those due to marrow aplasia (resulting from irradiation or toxins such as benzol), and those due to destruction of leucocytes in the spleen.

The technique for detection of leucocyte agglutinins is as follows. Into a 7-mm. siliconed tube is placed 1 ml. of 3% polyvinylpyrrolidone ("subtosan") containing 6 units of heparin, and 3 ml. of fresh blood is added. This is allowed to stand for 30 to 40 minutes at 37° C., after which the erythrocytes will have settled and the plasma, containing mainly platelets and leucocytes, can be removed. On a number of microscope slides (75 × 26 mm.) are affixed thick cover slips so as to leave a depressed chamber 26 mm. square. In one chamber one drop of leucocyte suspension is mixed with 3 drops of test serum, and in 4 other chambers one drop of the suspension is mixed with 3 drops of normal serum, one chamber being allotted to serum from each of the four blood groups. The 5 chambers are enclosed in a moist atmosphere and incubated for one hour, each then being covered by a thick coverglass (32 × 24 mm.) and the whole area examined for agglutinates. A drop of 6% acetic acid is then added to each side of the chamber and the area re-examined, the acid lysing the erythrocytes and making the leucocytes more evident. *George Discombe*

1059. **Bovine Antihaemophilic Globulin in the Treatment of Haemophilia**
R. G. MACFARLANE, R. BRIGGS, and E. BIDWELL. *Lancet* [*Lancet*] **1**, 1316–1319, June 26, 1954. 2 figs., 13 refs.

The rational treatment of haemophilia should be to raise the blood level of antihaemophilic globulin (A.H.G.) to the point at which coagulation can become haemostatically effective. It has recently been shown that at least 30 to 50% of the normal amount of A.H.G. in the blood is required for reasonable haemostatic efficiency. Up to the present the amounts of blood or A.H.G. usually given to haemophiliacs have been insufficient to produce really effective therapeutic levels, and although 2 to 5% will restore to normal the clotting time of the blood, this amount is usually not enough for the treatment of bleeding.

Working at the Radcliffe Infirmary, Oxford, the authors have found that ox blood has an average A.H.G. activity 16 times that of human blood, and they have been able to prepare material by salt fractionation from this source whose A.H.G. activity per g of protein is equivalent to that of 20 pints (11·4 litres) of normal blood. This material retains its activity indefinitely in the dried state, but quickly deteriorates in solution.

In tests of the substance made on 3 haemophilic volunteer subjects after preliminary skin tests for sensitivity had proved negative, 0·4 to 0·5 g. of the A.H.G. preparation was injected intravenously before and after the extraction of teeth. In 2 cases there was no abnormal bleeding; in the third case removal of 16 teeth caused bleeding for several hours, but this was not severe enough to necessitate blood transfusion.

No ill effects were observed in the first 2 patients, but in the third thrombocytopenia without purpura resulted. The bovine material agglutinated platelets in a concentration as low as 0·125 mg. per ml. of blood. Tests made on the patients' blood 3 and 6 weeks later showed that specific antibodies to A.H.G. had not developed to any significant extent.

The authors conclude that the results of this preliminary clinical trial are sufficiently promising to warrant further investigation. *A. Brown*

1060. **Researches on the Anaemia of Acute Leukaemia. I. The Metabolism of Iron in Acute Leukaemia Studied with the Help of Radioactive Iron.** (Recherches sur l'anémie des leucoses aiguës. I. Métabolisme du fer dans la leucose aiguë étudié à l'aide du fer 59)
G. SCHAPIRA, M. TUBIANA, J. C. DREYFUS, J. KRUH, M. BOIRON, and J. BERNARD. *Revue d'hématologie* [*Rev. Hémat.*] **9**, 3–26, 1954. 8 figs., 35 refs.

The authors have investigated the anaemia which occurs in acute leukaemia by studying the rate of incorporation of radioactive iron (^{59}Fe) into the erythrocytes and also its distribution among the various haemoglobin fractions. [For details of the methods and calculations used, the original paper should be consulted].

In 3 untreated cases of acute leukaemia they found that the plasma iron concentration returned to its original level at the normal rate following a dose of ^{59}Fe, and it was calculated that there was normal or increased utilization of iron. From this they conclude that haematopoiesis is normal or increased in acute leukaemia, and that aplasia is not the cause of the anaemia. On the

other hand the survival time of the erythrocytes was reduced and the curves obtained were of the same nature as those found in another case of acute leukaemia which was associated with gross haemolytic anaemia, whereas in a case of leukaemia in remission the erythrocyte survival curves were normal.

Fractionation of the haemoglobin by adsorption on alumina showed that in leukaemic subjects, even in remission, the rate of incorporation of ^{59}Fe into haemoglobin B was consistently higher than into haemoglobin A, whereas in patients with cancer, but without any blood disorder, the reverse was the case. It is suggested that this is the result of a disturbance of biosynthesis of haemoglobin caused by the leukaemic invasion of the marrow. *R. F. Jennison*

1061. **The Occurrence of Leukemia**
J. V. COOKE. *Blood* [*Blood*] **9**, 340–347, April, 1954. 2 figs., 8 refs.

Since leukaemia is always fatal the author analysed the deaths from this disease as reported by the United States Bureau of the Census for the years 1930–49 with the object of determining the incidence in the general population, particularly in relation to age. During the period under review there was a continuous rise in the number of deaths from leukaemia, from 2·1 per 100,000 in 1930 to 5·5 per 100,000 in 1949. Although there was some increase in all age groups, the most spectacular rise was observed in subjects aged 50 years and over, the increase being fivefold in the older age groups during the period under review.

The author considers that improved diagnostic facilities account for some of the increase in the younger age groups, but that the striking differential increase among older subjects must represent a real rise in the incidence of the disease in later life. This view is supported by the fact that recently published analyses of the age incidence of leukaemia show a percentage incidence in patients over 50 which is double that given in earlier reports. *P. C. Reynell*

1062. **The Causes and Prevention of Defective Function of Stored Red Blood Cells after Transfusion**
D. J. VALTIS and A. C. KENNEDY. *Glasgow Medical Journal* [*Glasg. med. J.*] **34**, 521–543, Dec., 1953. 8 figs., 11 refs.

The authors describe further experiments carried out at the Royal Infirmary, Glasgow, to elucidate their previous findings (*Lancet*, 1954, **1**, 119; *Abstracts of World Medicine*, 1954, **15**, 405) that the oxygen dissociation curve of blood stored in an acid citrate–dextrose medium is shifted to the left, the curve of the recipient's blood also being shifted to the left. The aim of the present investigation was to determine if possible the cause for this change.

It was shown that the cell *p*H may be responsible for the major part of the displacement of the oxygen dissociation curve to the left. The *p*H of the cells of citrated blood became greater than the *p*H of the plasma after storage; moreover, the *p*H of the recipient's cells showed a pronounced shift to the alkaline side after transfusion. The authors further demonstrated that the addition of 0·5% sodium chloride to the stored citrated blood restores the normal distribution of carbon dioxide and chloride between cells and plasma. The addition of sodium chloride to stored blood was often found to have a beneficial effect on the recipient's post-transfusion oxygen dissociation curve. *Kate Maunsell*

1063. **Kernicterus following Exchange Transfusion**
D. A. MCGREAL. *Lancet* [*Lancet*] **1**, 1323–1325, June 26, 1954. 11 refs.

In this paper from Dundee Medical School the author reports that although a number of workers have reported that the use of exchange transfusion in haemolytic disease of the newborn has greatly reduced the incidence of kernicterus, his personal experience has been less encouraging. During 1952–3, among 16 infants with haemolytic disease treated by exchange transfusion, there were 4 cases of kernicterus, 3 of these being in premature infants. (Two additional earlier cases, both in mature infants, are also mentioned but not described.) The histories of the 4 reported cases are given in some detail.

It is suggested that at present the maintenance of serum bilirubin levels as low as possible by repeated exchange transfusions offers the best hope of reducing the incidence of kernicterus. *A. Brown*

1064. **Potentially Dangerous Group-O Blood. A Screening Test**
J. M. GARDNER and G. H. TOVEY. *Lancet* [*Lancet*] **1**, 1001–1004, May 15, 1954. 5 refs.

A simple test, developed at the South-western Regional Transfusion Centre, Bristol, for the routine detection of the potentially dangerous "universal" donor in a busy blood bank is described. One volume of fresh donor serum (not more than 24 hours old; otherwise selected fresh human serum is added for the second stage of the test) is incubated with one volume of a 5% suspension in saline of erythrocytes of Groups A, B, and O (as a control) for one hour at 20° C. and then for one hour at 37° C. Two readings are made: (1) the serum agglutinin content after one hour, and (2) the degree of haemolysis after 2 hours. When strong haemolysis occurs, blood from the donor concerned is used for Group-O recipients only.

Samples of serum from 1,960 Group-O donors taken at random were examined and 185 found to contain strong anti-A or anti-B haemolysins. Of those with strong anti-A haemolysins, 10% also contained immune anti-A agglutinins in a titre of 1 in 16 or more, whereas when serum from 772 of the "safer" donors was examined by the indirect Coombs technique for immune anti-A agglutinins, none were found.

As the authors point out, "clinical and experimental investigations have not yest established whether the dangerous component of Group-O blood is the haemolysin or the immune agglutinin", but it is thought that the use of this test as a screening procedure will exclude all potentially dangerous Group-O donors.

I. Dunsford

Respiratory System

1065. **Antibiotic Combination in Treatment of Pneumococcic Pneumonia**

W. Weiss, G. M. Eisenberg, J. D. Alexander, L. Mann, and H. F. Flippin. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **154**, 1167–1170, April 3, 1954. 6 refs.

At Philadelphia General Hospital the authors have compared the relative efficacy of penicillin given intramuscularly and a mixture of equal amounts of chlortetracycline (aureomycin), oxytetracycline ("terramycin"), and chloramphenicol given orally in the treatment of 62 cases of pneumococcal pneumonia, 38 of which received the former and 24 the latter medication. Results showed that the two treatments were equally effective in controlling the infection. The 4 deaths which occurred (3 in the penicillin-treated group and 1 in the other) were due principally to causes other than pneumonia, being the result of cerebral vascular accident in 2 cases and of myocardial infarction in the other 2. The two groups of patients were largely comparable as to severity of the disease and period of time required for resolution, and in the incidence of complications.

The authors point out that one of the most interesting features of the study was the fact that of 283 cases admitted with an initial diagnosis of pneumonia, the great majority had to be eliminated from the trial for various reasons. For example, no fewer than 45 were shown to have pulmonary tuberculosis or pleural effusion, 24 had pneumonia due to *Klebsiella*, 19 were suffering from cardiac failure, and 10 from neoplasm. They also stress that the results emphasize the difficulty of assessing new therapeutic agents in the treatment of pneumonia, since accepted forms of treatment are now so efficient that pre-existing disease, generally of the cardiovascular or respiratory system, has become the most frequent cause of death in patients suffering from pneumonia.

J. G. Scadding

1066. **Nonspecific Lung Abscess: Experience with Fifty-five Consecutive Cases**

J. R. Fox, F. A. Hughes, and W. D. Sutliff. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **27**, 255–260, March, 1954. 2 figs., 9 refs.

The symptomatology in, and treatment of, 55 cases of non-specific lung abscess seen during the 6-year period 1947 to 1952 are discussed; cases in which the abscess was secondary to bronchiectasis, carcinoma, cyst, or tuberculosis were excluded. Over this period a marked increase was noted in the number of cases in which there were lesions affecting the right upper lobe—40% of the total—for which the authors can offer no explanation. Of 26 patients seen during the first 3 years of the period, 4 had symptoms which were minimal or not indicative, clinically, of an abscess; of the 29 seen in the second 3 years, 12 had minimal symptoms. The authors emphasize the value of bronchoscopy in all cases, not as a therapeutic measure but to exclude the presence of a tumour, foreign body, or other intrabronchial lesion. In all cases at least 1,200,000 units of penicillin were given daily, regardless of the stage of the disease, but it is noted that the longer the duration of symptoms the less was the response to chemotherapy. Of 32 patients given intensive antibiotic therapy alone, 28 recovered, 3 improved, and one died. The remaining 23 patients required surgical treatment in addition to administration of antibiotics; resection of the lesion was carried out in 19 of these, all of whom recovered, and primary drainage in 4, of whom 2 recovered, one improved, and one died.

W. P. Cleland

1067. **Bilateral Bronchiectasis.** (Beiderzijdse bronchiëctasieën)

J. Swierenga. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **98**, 1049–1056, April 17, 1954. 12 refs.

When bronchiectatic conditions associated with recognized causes such as congenital bronchial dilatation (honeycomb lung, bronchial cysts), tuberculous pneumonia, syphilis, bronchial stenosis due to tuberculous adenitis, tuberculous bronchitis, or tumours, and recurrent pneumonia are excluded, there remains a large group of cases of bronchiectasis, which is bilateral in about 30%, for which there is no evident cause. The condition may sometimes develop after pertussis or measles and particularly after the primary atypical and virus types of pneumonia. In the present author's opinion primary atypical pneumonia, which may be virtually symptomless, may be of considerable importance in the aetiology of the ordinary form of bronchiectasis, and for this reason the administration of chloramphenicol or aureomycin in such cases is advisable.

The treatment of bilateral bronchiectasis is essentially surgical and should not be delayed. The extent of the disease and disturbance of lung function will determine the possibility of bilateral resection. Where one side is severely and the other slightly affected it may be found that resection of the former is followed by clearing of the latter, while when both lungs are heavily involved it is best to operate on the lung least affected first, as with the reverse order death from anoxaemia may follow the second operation. Repeated antibiotic treatment is not recommended.

Out of a total of 450 cases of bronchiectasis treated by the author at St. Anthony's Clinic, Utrecht, by resection with careful preoperative and postoperative treatment with penicillin and chloramphenicol, 20 were bilateral cases, amongst which there was one operative death. Postoperative complications (mainly spread of infection to the opposite side and failure of the lung to expand) are discussed.

R. Crawford

Otorhinolaryngology

1068. **Causes of Deafness in Young Children**
E. P. FOWLER and M. BASEK. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **59**, 476–484, April, 1954. 4 figs., 13 refs.

In this study of the causes of permanent deafness in young children seen at the Vanderbilt Clinic and elsewhere in New York, the authors comment on the change which has come about in the attribution of causation of deafness. In 1928, for example, the list of causes was dominated by meningitis and scarlet fever, and a further large group of cases was attributed to unknown causes. In another study carried out in 1937, 61% of cases were described as congenital, and 41% of these as hereditary.

In the present series of 270 children, in all of whom deafness appeared before 5 years of age, the defect was thought to be due to prenatal causes in 81 and to postnatal causes in 189. The former group included 7 cases of dominant-recessive hereditary deafness, and of 50 cases due to causes during pregnancy, 12 were due to Rh incompatibility, 12 to maternal measles, and 2 to the use of abortifacients. Of 21 cases due to causes during labour, birth trauma accounted for 13, and 4 resulted from postnatal cyanosis. The authors suggest that "emotional causes" with excessive vomiting in the mother may be an intra-uterine factor; in the present series 7 of the cases were associated with excessive maternal vomiting. Prenatal medication of the mother may also cause deafness in the child, and the 2 cases in which the defect seemed to have been due to attempts at abortion strengthen this view. On the other hand 2 children born to mothers who were receiving streptomycin for tuberculosis showed no deafness and no vestibular lesion.

Of the 189 children whose deafness was attributed to postnatal causes, no definite cause could be found in 86. The authors point out that many children with hereditary deafness have very little deafness at birth, but degeneration of the inner ear develops rapidly during the first few months of life—as in the well-known waltzing mice and congenitally deaf dogs and cats of the classic dominant Mondini type. Of the remaining 103 cases, 45 were due to otitis media, 26 of these being described as "catarrhal". As the authors suggest, probably in most of these cases antibiotics and chemotherapy had reduced an originally suppurative process to a "catarrhal" one, and they describe as "a most fallacious idea" the belief that because an infection is cleared up myringotomy and mastoidectomy are no longer required to preserve hearing. (They cite the cases of 3 patients who came to the clinic with a diagnosis of "fulminating" otosclerosis and a recommendation as candidates for "endaural fenestration"; all 3 were relieved by myringotomy.) There were no cases of otosclerosis in the series, but 3 of the patients had a condition indistinguishable from Ménière's disease. There were 8 cases of unilateral total deafness following mumps, and since these figures were collected the authors have seen a 3-year-old child with total bilateral deafness following mumps—fortunately a very rare event. *F. W. Watkyn-Thomas*

1069. **Papillary Cystadenoma of the Maxillary Paranasal Sinus (Atypical Warthin Tumor)**
A. M. STRUTHERS, H. L. WILLIAMS, and E. M. PARKHILL. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **59**, 241–244, Feb., 1954. 3 figs.

The literature contains reports of 303 cases of single or multiple Warthin tumours, the tumours being near or within the parotid gland in 275 of the cases, and in the vicinity of the submaxillary salivary gland in 10; in all the cases the tumour arose in the area where branchial cleft remnants are found. In the present paper from the Mayo Clinic the authors describe a case of papillary cystadenoma of the maxillary paranasal sinus (atypical Warthin tumour); they believe that this is the first case of its kind to be reported. It is pointed out that the developing maxillary bone is in close association with the bifurcation of the first branchial arch.

The patient, a woman of 69, had had haemorrhage from the left nostril for 3 years. On examination a polypoid mass was found in the left nasal fossa. Radiographs of the skull and paranasal sinuses revealed clouding of the left side of the nose, antrum, and ethmoid, but no evidence of bone destruction. A Caldwell–Luc operation was carried out, and transantral exploration of the left ethmoidal sinus revealed a mass attached to the antral wall in the region of the middle meatus and extending into the ethmoid. After removal of the mass the antral mucosa appeared to be normal and intact. On the pathological findings an "atypical Warthin tumour of the left maxillary sinus" was diagnosed.
F. W. Watkyn-Thomas

1070. **Malignant Disease of the Superior Maxilla**
C. P. WILSON. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **14**, 285–302, May, 1954. 9 figs.

LARYNX

1071. **Tumor Involving the Laryngeal Cartilages**
A. EHRLICH. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **59**, 178–185, Feb., 1954. 7 figs., 3 refs.

Hyaline cartilage is a form of connective tissue which is sparsely supplied with blood and lymph vessels; for this reason it would be expected that tumour metastases to such tissue would be rare. On the other hand, bony metaplasia of the laryngeal cartilages is common and

tumour metastases to bone are frequently found. The present author, in a review of the literature, did not find a single case report of metastasis to the laryngeal cartilage. He now describes 5 cases of metastasis to the thyroid and cricoid cartilages from carcinomata and 3 others of involvement of these cartilages in leukaemia or multiple myeloma which were found in a series of 100 consecutive necropsies carried out at Montefiore Hospital, New York. The laryngeal involvement was secondary to bronchogenic carcinoma in 2 cases, to carcinoma of the prostate in one, and to mammary carcinoma in 2. Of the remaining 3 patients, 2 had myelogenous leukaemia and one had multiple myeloma. In all cases there was metaplastic bone formation in the cartilages with generalized metastatic involvement of bone. *F. W. Watkyn-Thomas*

1072. **Cancer of the Larynx. Laryngoplasty to Avoid Laryngectomy**

J. J. PRESSMAN. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **59**, 395–412, April, 1954. 17 figs., 30 refs.

Recent advances in the surgical treatment of cancer of the larynx have been towards the establishment of a normal airway and a " natural ", if not a normal, voice. To remove almost the entire larynx and yet maintain a normal airway it is necessary to (*a*) provide a lining, (*b*) maintain a lumen, and (*c*) impart rigidity to the whole. The author, in an operation which he calls " laryngoplasty " and which is here described from the University of California Medical Center, Los Angeles, uses the external perichondrium of the thyroid alae as the lining, provides an obturator for the lumen, and transplants the cartilage of the alae to a new position to ensure rigidity. By these measures the whole laryngeal contents, that is, the true and false cords, ventricles, and one arytenoid, can be removed, with portions of the circumference of the cricoid, several tracheal rings, and the pre-laryngeal soft tissues of the cricothyroid area; the posterior segment of the cricoid is not removed, as this would interfere too much with the action of the aryepiglottic folds which protect the larynx during swallowing.

The operation is described in stages, as follows. (1) After preliminary tracheotomy, the sternohyoid muscles are exposed and a pocket made between them and the deeper ribbon muscles. (2) The perichondrium —which will become the lining of the new larynx—is stripped off the thyroid cartilage and stitched to the deep layer of ribbon muscles, the sternohyoid, and thyrohyoid, this being done *pari passu* with reflection of the perichondrium. (3) The thyroid cartilage is split and the soft structures of the larynx stripped off until the cornua are freed and the entire length of the posterior margin reached; the cartilage is removed, and kept for transplanting. (4) The diseased area of the laryngeal lining is freely removed. (5) The edges of the mucosa are stitched to the perichondrial muscle flaps. (6) The pieces of thyroid cartilage are tucked into the pockets made at Stage 1 and are fixed by through-and-through sutures to the new laryngeal wall. (7) An obturator—usually a polythene tube—is put into the new lumen, secured by tantalum sutures through the new laryngeal wall and skin, and the larynx closed over it. (8) As a last stage, the base of the epiglottis and the adjacent soft structures are pulled up and anchored to the hyoid to prevent them from forming a " flap valve " as they might otherwise do, the support of the thyroid cartilage having gone.

After operation the obturator is left in place for about 6 weeks, it being hoped that in this time mucosa will have grown over the whole inner surface. In some cases a cicatricial " vocal cord " forms, which improves phonation. The main complicating difficulties are recurrent oedema and stenosis of the new larynx; in some cases it may be necessary to insert the obturator again after 6 months for another 6 weeks. The operation is indicated mainly in cases in which laryngofissure or hemilaryngectomy would be inadequate, and especially in cases of limited subglottic disease, which give a poor response to irradiation. (In the interesting discussion which followed the paper it was reported that in 14 cases in which this operation had been performed there had been only 2 failures; but it was stressed that the procedure was only for carefully selected cases and for experienced operators. A big advantage of the technique is the avoidance of skin flaps and all the difficulties which they entail.) *F. W. Watkyn-Thomas*

1073. **Emergency Laryngectomy**

W. B. HOOVER and G. D. KING. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **59**, 431–433, April, 1954. 1 ref.

In this paper from the Lahey Clinic, Boston, the authors point out that it is so generally accepted that laryngectomy should not be performed without preliminary biopsy that, if a patient reaches hospital with respiratory obstruction, tracheotomy is usually carried out at once often under difficult conditions and without regard to the risk of transecting malignant tissue situated, for example, in the thyroid isthmus or in a subglottic or tracheal extension. If later laryngectomy is necessary, it has to be performed through a contaminated field and the tracheal stump is difficult to manage neatly owing to the recent tracheotomy.

The authors therefore recommend that if an experienced observer decides by mirror examination that carcinoma is present, and if the chest is clear clinically and radiologically, a diagnosis of carcinoma is justified and a definitive operation should be attempted. Under intravenous anaesthesia an endotracheal airway is inserted immediately to relieve the acute obstruction, and then wide-field laryngectomy, with neck dissection if necessary, is carried out. Two cases are described, in one of which operation was performed 3 hours after admission to hospital and in the other 11 hours after. Both patients recovered.

The authors conclude as follows: " We believe that airway obstruction secondary to cancer is an emergency and that the relief of obstruction can, in selected cases, be incorporated with the definitive curative procedure of laryngectomy ".

F. W. Watkyn-Thomas

Urogenital System

1074. **Electrolyte Balance in Acute Renal Insufficiency. Changes in Plasma Anions.** (Équilibre électrolytique de l'insuffisance rénale aiguë. Modifications des anions plasmatiques)
M. Dérot, P. Pignard, M. Miocque, M. Legrain, and J. J. Bernier. *Presse médicale* [*Presse méd.*] **62**, 704–706, May 5, 1954. 1 fig., 30 refs.

The authors report their observations on more than 200 patients in acute renal failure seen during 6 years at the Hôtel-Dieu, Paris. Comprehensive blood analyses were made in every case, including daily estimation of electrolyte levels [but the paper contains only one table showing single determinations only of the plasma concentration of sodium, total cations, protein, chlorine, carbon dioxide, sulphate, phosphate, and total anions in 24 of the cases, although the conclusions reached by the authors are obviously based on the results of the determinations in all the cases].

Hypochloraemia, which was more frequent than hyponatraemia, may be due to chloride passing from the extra- to the intra-cellular fluid. No simple relation was apparent between a low alkali reserve and acidosis. Inorganic sulphate and phosphate levels were raised, thus partly compensating for the low alkali reserve and the hypochloraemia. The level of organic sulphur compounds, on the other hand, was raised only slightly and rarely sufficiently to support the hypothesis that these substances form detoxicated compounds with toxic metabolites. It is concluded that anions play the major role in maintaining the acid–base equilibrium of the plasma.

L. H. Worth

1075. **Late Results of Transplantation of Ureters into the Pelvic Colon**
A. Jacobs. *British Medical Journal* [*Brit. med. J.*] **1**, 1340–1342, June 12, 1954. 2 refs.

In this paper from the Royal Infirmary, Glasgow, the author states that the late results of uretero-colic anastomosis depend upon the type of lesion, on the continued integrity of the upper urinary tract, and on the effects of any electrolyte imbalance which may develop, these observations being based on a careful follow-up study of 162 personal cases and a previous survey, with Stirling (*Brit. J. Urol.*, 1952, **24**, 259; *Abstracts of World Medicine*, 1953, **13**, 487), of 1,673 cases.

In cases of malignant disease, in which transplantation may be part of a curative or merely a palliative procedure, the late results after transplantation are bad, 61% of patients dying within 3 years. Good results are obtained in cases of early carcinoma of the bladder with minimal infiltration—but similar results may be obtained by conservative measures. The author now reserves transplantation and cystectomy for cases of widespread, multiple, non-penetrating tumours and for those with broad-based, sessile, papillary growths in the lower zones, or as a palliative measure for tumours that have penetrated and are causing bleeding and much pain. In cases of renal tuberculosis transplantation of the remaining ureter gives a good measure of relief. The author uses Leadbetter's modification of Nesbit's operation, the results of which have been good, particularly in cases of contracted bladder accompanied by persistent frequency of micturition.

The survey referred to above showed that some 50% of patients develop some degree of electrolyte imbalance postoperatively. The author comes to the conclusion that the capacity to deal with selective absorption from the bowel is related closely to the state of renal function, and that almost always chemical imbalance was found to be associated with dilatation of the upper urinary tract and a high blood urea level. Minor degrees of imbalance are readily corrected with alkalis and restriction of salt intake. He does not agree that the use of a segregated tube of ileum will prevent renal damage which is due to faulty anastomosis with the bowel.

K. H. Taylor

1076. **Renal Papillary Necrosis**
D. Swartz. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **71**, 385–397, April, 1954. 15 figs., 11 refs.

The author describes 3 cases of renal papillary necrosis (necrotizing papillitis), 2 of which, in diabetic adults, were diagnosed during life and were successfully treated by unilateral nephrectomy. The third was an incidental finding at necropsy on a 5-month-old girl dying of meningitis due to *Pseudomonas aeruginosa*.

J. B. Enticknap

1077. **Nephrocalcinosis: a Collective and Clinicopathologic Study**
J. Mortensen and J. L. Emmett. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **71**, 398–406, April, 1954. 5 figs., 21 refs.

The authors define nephrocalcinosis as " roentgenographically demonstrable diffuse renal parenchymal calcification ", and have collected 48 cases from the literature and a further 43 from the records of the Mayo Clinic. The primary cause was recognizable in 84% of cases, primary hyperparathyroidism, hyperchloraemic acidosis, and chronic pyelonephritis together accounting for 75%. No characteristic signs or symptoms other than those of the causative disorders were recognized.

J. B. Enticknap

1078. **The Treatment of Urinary Infections with " Furadantin ".** (De behandeling van urineweginfecties met furadantine)
A. J. C. Haex and A. J. Z. Voorspuij. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **98**, 1357–1360, May 15, 1954. 9 refs.

Endocrinology

1079. **Plasma-insulin Activity in Acromegaly Assayed by the Rat-diaphragm Method**
P. J. RANDLE. *Lancet* [*Lancet*] **1**, 441–444, Feb. 27, 1954. 9 refs.

At Addenbrooke's Hospital and the University of Cambridge the insulin activity of the blood of acromegalic patients with diabetes was compared with that of a control group of healthy subjects. The plasma insulin level was determined by the method of Groen *et al.* (*J. clin. Invest.*, 1952, **31**, 97), which is based on the glucose uptake of the isolated normal rat hemidiaphragm surviving *in vitro*.

Plasma was taken from 2 acromegalic diabetic patients during insulin therapy (4 and 27 hours respectively after the last injection) and from a similar patient who was not receiving insulin. The quantitative determination of the glucose uptake of the rat hemidiaphragm in the presence of normal and acromegalic plasma showed that the latter possessed a much greater insulin activity. The difference was significant, even when the acromegalic plasma was diluted 1:50 and 1:100.

In view of the claim of Bornstein and Lawrence that the plasma of diabetic acromegalic patients when injected into the alloxan-diabetic hypophysectomized adrenalectomized rat causes hyperglycaemia, the effect of a sample of diabetic acromegalic plasma upon an alloxan-diabetic hypophysectomized (A.D.H.) rat was studied. The insulin activity of this plasma was simultaneously assessed by the rat-diaphragm method, and though it contained 41 milliunits of insulin per ml., there was no fall in the blood sugar level of the A.D.H. rat. However, 2 milliunits of insulin given to an A.D.H. rat caused a significant fall in the blood sugar level.

The author considers that the increased insulin-like activity of acromegalic plasma, as assayed by the rat-diaphragm method, does not necessarily mean that the plasma contains more insulin than normal; the growth hormone found in acromegalic plasma (Ottaway, *Brit. med. J.*, 1953, **2**, 357; *Abstracts of World Medicine*, 1954, **15**, 243) might be responsible. Until the nature of the causative factor is known—and further investigations of this are being carried out—the significance of the author's findings cannot be assessed. *Richard de Alarcón*

See also Pathology, Abstract 916.

1080. **Syndrome Characterized by Galactorrhea, Amenorrhea and Low Urinary FSH: Comparison with Acromegaly and Normal Lactation**
A. P. FORBES, P. H. HENNEMAN, G. C. GRISWOLD, and F. ALBRIGHT. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **14**, 265–271, March, 1954.

The authors describe and discuss 15 cases seen at Massachusetts General Hospital in the last 10 years presenting a syndrome characterized by galactorrhoea, amenorrhoea, and a low urinary excretion of follicle stimulating hormone (F.S.H.). The laboratory and clinical findings in the cases are summarized in a table. Of the 15 women, 9 had never been pregnant, but in 2 of them the onset of galactorrhoea had coincided with pseudocyesis. Most of the patients were aged about 24 or 25 when the condition developed, and almost all had some degree of hirsutism, obesity, and seborrhoea. In all but one case the urinary excretion of F.S.H. was subnormal. Of 7 of the women given courses of progesterone, only one showed withdrawal bleeding, indicating that the others had an oestrogen deficiency; in most of the cases the excretion of 17-ketosteroids was higher than normal.

The authors suggest that the condition is most probably of pituitary origin, since in 8 of the 15 cases there was evidence of pituitary tumour and biopsy examination in 3 of these revealed a chromophobe adenoma. Pituitary dysfunction would also explain the subnormal excretion of gonadotrophin and consequent oestrogen deficiency. The serum phosphorus concentration was normal in all cases, and there were no signs of acromegaly which, when associated with amenorrhoea, often causes lactation. Nor were the conditions like those in normal lactation, even though some of the patients had started by having a normal lactation which then persisted for several years. A study of 9 normal lactating women with and without amenorrhoea showed that gonadotrophin excretion was normal or high, and only one of these failed to show withdrawal bleeding after progesterone treatment. Oestrogen deficiency, then, obviously does not cause the lactation, since if it did this would occur after ovariectomy or the menopause. Treatment with oestrogen may restore normal menstruation in these cases, but it has little or no effect on the galactorrhoea.

The authors conclude that overproduction of prolactin is the most probable cause of this syndrome. Cushing has stated that the cells of chromophobe adenomata are pre-eosinophil cells and that lactation often accompanies acromegaly in which there is eosinophil-cell overactivity. Tumour pressure would account for the lack of gonadotrophin, but most of these patients showed no evidence of over-all pituitary deficiency. *Peter C. Williams*

1081. **Hypoparathyroidism and Pseudohypoparathyroidism**
R. R. DE MOWBRAY, S. H. L. SMITH, and W. J. C. SYMONDS. *British Medical Journal* [*Brit. med. J.*] **1**, 903–909, April 17, 1954. 7 figs., 48 refs.

It is first pointed out that idiopathic hypoparathyroidism is a rare condition, only 3 cases having been reported in the British literature. Pseudohypoparathyroidism, in which the parathyroid glands are normal or even hyperplastic but there is resistance to parathyroid hormone, is rarer still. The authors report 3 cases of idiopathic

hypoparathyroidism and one of pseudohypoparathyroidism from Guy's Hospital and Lewisham General Hospital, London. They also report 3 cases of hypoparathyroidism following thyroidectomy, which is a well-known complication.

In normal subjects and in patients with any form of true hypoparathyroidism a phosphate and water diuresis follows administration of parathyroid hormone, as shown by the Ellsworth–Howard test. The absence of this response in most cases of pseudohypoparathyroidism serves to distinguish the latter from true atrophy of the parathyroid gland. Pseudohypoparathyroidism is associated with dyschondroplasia and subcutaneous calcification or bone formation, all defects being probably genetically determined.

The clinical and biochemical findings are described in detail. The varying presenting symptoms referable to hypocalcaemia, which include tetany, epilepsy, loss of hair, defects in growth of teeth and nails, cataract, papilloedema, and other neurological symptoms, are emphasized.

The treatment of choice is the administration of dihydrotachysterol or calciferol. On theoretical grounds the former is preferable because it more closely resembles parathyroid hormone, but in practice there is little to choose between the two drugs. Dihydrotachysterol is, however, expensive, while calciferol is apt to induce hypercalcaemia. Calcium is required only in cases of acute hypoparathyroidism. *Nigel Compston*

THYROID GLAND

1082. **New Observations on the Endocrine–Metabolic Equilibrium in Endemic Cretinism.** (Nouvelles acquisitions sur l'équilibre endocrino-métabolique du crétinisme endémique)

A. COSTA, F. COTTINO, G. M. FERRARIS, E. MARCHIS, F. MAROCCO, M. MORTARA, and R. PIETRA. *Annales d'endocrinologie* [*Ann. Endocr.* (*Paris*)] **14**, 995–1011, 1953. 4 figs., 24 refs.

Full metabolic studies were carried out on 20 cases of endemic cretinism under treatment at the Mauriziano Hospital, Turin. The ages of the patients varied from 26 to 75 (average 56) years, and their heights ranged from 118 to 180 cm., the majority being toward the lower end of this range. Nodular goitres were present in most cases and were sometimes calcified; there were no clinical or electrocardiographic signs of myxoedema, but the pituitary fossa was smaller than normal in each of 10 cases examined.

Endemic cretinism was found to differ from other forms of hypothyroidism in the following important respects. (1) The basal metabolic rate (B.M.R.) was subnormal in only one case, while in 3 cases it was normal and in 10 it was actually raised (mean +23·6%). (2) The serum cholesterol level was raised in only 3 cases, in 10 cases it was normal, and in 6 it was reduced. (3) The serum protein-bound iodine level was not necessarily low; in 9 cases it was subnormal, in 10 it was normal, and in one case it was raised, the values ranging from 2·9 to 8·9 μg. per 100 ml. (mean 4·5 μg. per 100 ml.). (4) The uptake of radioactive iodine (^{131}I) by the thyroid gland was increased even above the levels found in cases of hyperthyroidism, although in contrast with the latter the rate of excretion of ^{131}I was slow. The mean uptake was 49·2% (normal 18%) after one hour and 49% (normal 30%) after 24 hours. The level of protein-bound ^{131}I in the blood varied from 43 to 77% of the total plasma ^{131}I (normal mean 13·6%), this finding being in contrast to the abnormally low level and slow uptake found in regions where iodine prophylaxis is practised. (5) The thyroid gland could be saturated with iodine as readily as could the normal gland, but this did not apply in cases of hyperthyroidism. Thus the intravenous injection of a solution containing 1 g. of sodium iodide, which was without effect upon the uptake of ^{131}I by the hyperthyroid gland, promptly inhibited the uptake in normal and cretinous subjects, even though the latter showed even higher initial uptakes than the hyperthyroid patients.

The thyroid gland was extremely sensitive to thyroid stimulating hormone (T.S.H.). After the administration of 20 mg. of T.S.H. daily for 3 days the B.M.R. was raised in 7 out of 10 cretins from a mean of +17·8% to a mean of +28·3%, compared with a rise from −2·6% to +1·52% in 5 normal subjects. The uptake of ^{131}I by cretins, however, was not significantly increased by T.S.H., though it was so increased in normal subjects. The plasma protein-bound iodine level, on the other hand, was more strikingly increased by T.S.H. in cretins than in normal persons (from a mean of 5·35 to 12·3 μg. per 100 ml. in the former and from 6·35 to 9·34 μg. per 100 ml. in the latter). Chromatographic analysis showed the presence of diiodotyrosine and thyroxine in the serum after the administration of ^{131}I, and the rise in the protein-bound iodine level was followed by a rise in B.M.R. and a fall in the serum cholesterol level, indicating that the output of hormonal iodine had been increased.

Treatment with thyroid extract was followed by increased mental alertness, loss of weight, a rise in B.M.R., and a diminution in the size of the thyroid gland and of its uptake of ^{131}I. *Robert de Mowbray*

1083. **Incidence of Malignancy in Toxic and Nontoxic Nodular Goiter**

J. E. SOKAL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **154**, 1321–1325, April 17, 1954. 11 refs.

The author, at the Yale University School of Medicine, has analysed statistics from the leading clinics in the U.S.A. over the past 20 years to estimate the incidence of thyrotoxicosis, carcinoma of the thyroid, and diffuse and nodular goitre and their various interrelationships.

His analysis shows that carcinoma is 20 times commoner in hyperthyroid patients than in euthyroid subjects. Thyroid nodules are pre-malignant lesions, cancer occurring in 1% of toxic nodular goitres, but in non-toxic nodular goitre the incidence is less than 0·2%. That carcinoma of the thyroid is 2 to 3 times more common among women than among men is explained by the fact that thyroid nodules are also 2 to 3 times as common in women.

The author's most practical conclusion is that the likelihood of patients with non-toxic nodular goitre developing cancer in the gland over the course of their lifetime is less than 1%, and of those with diffuse goitre even less. *G. S. Crockett*

1084. **Identification of the Effects of Thyroxine Mediated by the Hypophysis**
H. EARTLY and C. P. LEBLOND. *Endocrinology* [*Endocrinology*] **54**, 249–271, March, 1954. 21 figs., 44 refs.

The effects of varying doses of thyroxine on hypophysectomized or thyroidectomized rats were studied at McGill University, Montreal, and compared with those on intact animals. The hypophysectomized animals ceased to grow, and did not gain significantly more weight on doses of 6 μg. of thyroxine daily than animals not given the hormone. Thyroidectomized animals, on the other hand, continued to grow at a reduced rate for 10 days after operation, but growth then remained stationary; in these animals doses of 3 to 6 μg. of thyroxine restored full growth, but a larger dose (12 μg.) raised the oxygen consumption above normal and only partially restored growth. Oxygen consumption was reduced in the thyroidectomized rats, and even more in the hypophysectomized animals. In both groups it was restored to normal by thyroxine, but a dose of 3 to 6 μg. raised it to higher levels in the thyroidectomized than in the hypophysectomized animals, although the effects of a dose of 12 μg. of thyroxine were similar in both groups. The heart rate, which was depressed, was increased according to the dose of thyroxine given, and there was no significant difference in response between the thyroidectomized and hypophysectomized animals.

Study of the effects on non-endocrine organs showed that the absolute weights of these organs were reduced in the operated animals. Treatment with thyroxine restored them to normal in the thyroidectomized animals, but had a less marked effect in the hypophysectomized animals, although the organ weights relative to body weight were raised to the level found in the intact controls. The diameter of the proximal convoluted tubules of the kidney was decreased in the thyroidectomized, and even more in the hypophysectomized, animals. Thyroxine restored the tubule diameter completely in the former, but increased it only to a very small extent in the latter. The epidermis was thicker in both groups of operated animals as compared with the intact controls, and in both it became less thickened with thyroxine.

The endocrine organs were atrophic in the hypophysectomized animals. In the thyroidectomized rats the testicles were atrophic to a lesser extent; in these animals the weight of the testicles and the histological appearance of the renal tubules and interstitial tissue were maintained by thyroxine, but in the hypophysectomized rats the testicular weight diminished still further and vacuoles appeared in the Sertoli cells. The weight of the adrenal glands was increased in the thyroidectomized animals by treatment with thyroxine, but not in the hypophysectomized animals. The pituitary gland of the untreated thyroidectomized rats showed a complete lack of acidophil cells, which was corrected by thyroxine. This suggested that thyroxine may release growth hormone from the hypophysis, and the findings in regard to the testes and adrenals also suggested that it might release gonadotrophins and corticotrophin.

Thus there appear to be three types of thyroxine action: (1) a direct action upon oxygen consumption, heart rate, and thickness of the epidermis, which is independent of the hypophysis; (2) effects upon body growth, sexual development, and growth of the adrenals, mediated by the hypophysis; (3) a combination of direct action and mediation by the hypophysis in stimulating growth of the non-endocrine organs. *Robert de Mowbray*

See also Tuberculosis, Abstract 988.

PANCREAS

1085. **A Hyperglycaemic and Glycogenolytic Nucleoprotein from the Pancreas.** (Ein hyperglykämisierendglykogenolytisches Pankreasnucleoproteid)
G. MOHNIKE and H. BOSER. *Zeitschrift für die gesamte experimentelle Medizin* [*Z. ges. exp. Med.*] **123**, 415–433, 1954. 4 figs., 44 refs.

The authors report from the Garz Diabetic Hospital, Karlsburg, Germany, the isolation of a crystalline pancreatic extract, free from insulin and having an isoelectric point of 4·85 and the general structure of a nucleoprotein. Its zinc content was less than 0·02%. Injected intravenously into rabbits, this preparation showed distinct hyperglycaemic activity, approximately equal to that produced by half the same amount of adrenaline. Experiments with liver slices *in vitro* showed that the preparation was glycogenolytic, that it lost its activity very rapidly on being stored, but that this activity could be partly restored by the addition of cysteine. By means of the liver-slice technique, it was also found that a number of commercial insulins contained significant amounts of the hyperglycaemic factor. *B. Nordin*

1086. **The Renal Excretion of Inositol in Normal and Diabetic Human Beings**
W. H. DAUGHADAY and J. LARNER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **33**, 326–332, March, 1954. 5 figs., 10 refs.

At Washington University School of Medicine, St. Louis, the authors have studied the renal excretion of inositol by normal subjects and diabetic patients, the plasma and urinary inositol content being determined by the yeast microbiological test.

The daily urinary excretion of inositol by 11 non-diabetic subjects averaged 37 mg. (range 8 to 144 mg.), but that of 7 diabetic patients ranged from 280 to 851 mg.; in the latter group the diabetic inosituria disappeared when the glycosuria was brought under control. Ingestion of 3 g. of inositol caused the average plasma inositol level of 3 diabetic and 5 non-diabetic subjects to rise respectively from 0·60 to 2·47 mg. and from 1·02 to 1·72 mg. per 100 ml. in 4 hours; the corresponding average increases in urinary excretion of inositol on the

day of ingestion were 405 and 23 mg. respectively. After the slow intravenous administration of 20 mg. of inositol per kg. body weight the diabetic subjects excreted three times more inositol than the non-diabetics, but the plasma levels of dialysable inositol in the two groups were the same.

The renal clearance of inositol by 3 normal subjects with physiological plasma levels of inositol was low, but loading with glucose intravenously induced a 30-fold increase in inositol excretion; at high plasma inositol levels clearance rose to the level of endogenous creatinine clearance. The renal clearance of inositol by diabetic subjects was high even at normal plasma inositol levels. It is concluded that inositol is reabsorbed by a renal tubular mechanism and that high glucose loading inhibits the tubular transport of inositol. Inosituria of diabetes mellitus is attributed to increased inositol clearance produced by glycosuria rather than by polyuria.

J. E. Page

ADRENAL GLANDS

1087. **Further Studies on the Treatment of Congenital Adrenal Hyperplasia with Cortisone. V. Effects of Cortisone Therapy on Testicular Development**

L. WILKINS and J. CARA. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **14**, 287–296, March, 1954. 7 figs., 13 refs.

Previous work has shown that after cortisone therapy female pseudohermaphrodites suffering from adrenal hyperplasia develop female secondary characteristics and may start menstruation if the patient is more than 8 years old. In younger patients the results of treatment on sexual development are slight or *nil*. The onset of adolescent development depends on somatic (bone) age and not on chronological age.

In the present paper from Johns Hopkins Hospital, Baltimore, similar findings in boys with macrogenitosomia praecox are recorded. Of the 7 boys of chronological age of 3 to 8, but whose bone age was 9 to 14, all had high rates of 17-ketosteroid excretion (8 to 40 mg. per day) and equivalent development of secondary sex characteristics. The testes, however, in all of them were of pre-adolescent size, and biopsy in 6 cases showed undifferentiated cells in the tubules, with spermatogonia, few or no spermatocytes or Sertoli cells, and no Leydig cells. Treatment with cortisone reduced the 17-ketosteroid excretion to below 4·5 mg. per day in 6 of the boys and to 7 mg. in the seventh. The testes did not enlarge and there was no change in testicular structure in the 3 boys with bone ages of 9 to 10½ years, but some enlargement and increased seminiferous differentiation occurred in a boy with a bone age of 11 years, though no Leydig cells appeared. Full testicular maturation with enlargement to adult size, spermatogenesis, and Leydig-cell development occurred in the remaining 3 boys, whose bone ages were 11 to 14 years. There was increased virilization in these cases but not in those with no testicular changes. One of the patients had a nodule of aberrant adrenal (reticular-zone) tissue in one testis.

The authors suggest a probable explanation of the mode of action of cortisone. The excess of oestrogen and androgen secreted by the hyperplastic adrenal inhibits pituitary gonadotrophin secretion, although the androgen may cause some degree of seminiferous development. Cortisone, by suppressing the adrenal overactivity, releases the inhibited secretion of gonadotrophin. Cortisone has no direct effect on the testes in patients with other disorders. It also appears that somatic development must have reached a certain stage (in the present cases a bone age of 11 to 13 years) before the testes become responsive to gonadotrophin. Corroborative evidence for this was provided by the cases of 2 boys from whom virilizing adrenal tumours were removed; in both the 17-ketosteroid excretion was markedly reduced, but no change in testicular size or structure occurred in one boy whose bone age was 5½ years, whereas testicular enlargement and maturation occurred in the other, whose bone age was 12 years.

Peter C. Williams

1088. **Female Pseudohermaphroditism: Response to Cortisone Therapy**

R. VINES and L. DODS. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **3**, 5–17, Feb., 1954. 15 figs., 13 refs.

The authors describe, from the Royal Alexandra Hospital for Children, Sydney, the results of the treatment with cortisone of 6 cases of female pseudohermaphroditism due to adrenocortical hyperplasia. Four of the patients were aged 16, 9, 7, and 5 years respectively, the other 2 being infants aged 10 weeks when treatment was begun. The 4 older girls were given cortisone by mouth in large doses, the total varying from 25 to 150 mg. daily. They all showed marked clinical and psychological improvement. The first changes to become apparent were diminution in the acne and development of the breasts, the latter beginning within 2 to 6 months of the start of treatment in all 4 patients and progressing steadily thereafter, while the 2 oldest girls began to menstruate in 5 to 7 months. The level of 17-ketosteroid excretion was high in all 4 cases, but fell to levels which were approximately normal for girls of a corresponding stage of development, rather than for girls of the same chronological age.

The 2 infants were treated because of emaciation, vomiting, and marked enlargement of the clitoris. One responded satisfactorily to cortisone by mouth in doses which varied between 7·5 and 30 mg. daily, but the other continued to show signs of severe adrenocortical insufficiency and was treated by intramuscular injection of 15 mg. of cortisone on alternate days and 8 mg. of deoxycortone daily, together with an additional 4 g. of salt daily. Side-effects such as moon-face and increase of weight were not severe, and in no case did virilism develop. It is suggested that cortisone therapy should be started by the parenteral route, since reduction of 17-ketosteroid excretion is thus more reliably achieved and smaller doses of the hormone are required by this method.

The results in 5 of these cases are regarded as highly satisfactory, particularly in their psychological effects on the older girls, but how long cortisone therapy will have to be continued is not yet known. *A. C. Crooke*

The Rheumatic Diseases

1089. **Clinical Experience with a Rubidium–Gold–Creatinine–Gold Preparation in Rheumatic Diseases.** (Klinische Erfahrungen mit einem Rubidium–Gold–Kreatinin–Gold-Präparat bei rheumatischen Erkrankungen)
W. POHL. *Medizinische* [*Medizinische*] 659–661, No. 18, May 1, 1954. 9 refs.

The preparation used in this trial carried out at the University Polyclinic, Jena, was "aurubin", which is supplied as dragees consisting of small quantities of rubidium auritetrachloride, creatinine hydrochloride and aurochlorate, and other salts. The content of gold is less than that previously used by the author, the quantity of gold administered in an 8-week course of treatment amounting to only 0·306 g. The trial was conducted for a period of 3 to 4 months on 42 rheumatic patients. In general, the results obtained seemed to depend on the stage of the disease reached; it was also found that the dosage used must not be too rigid, but should be adjusted according to the reaction of the patient. A number of cases improved that had previously remained completely resistant to all forms of therapy.

Of the 42 patients, 21 were suffering from chronic polyarthritis, and of these 10 improved both subjectively and objectively, including 3 who had previously derived no benefit from the administration of cortisone or ACTH (corticotrophin). Of a further 7 patients suffering from Bechterew's disease (spondylitis deformans), 3 responded well, as also did 5 of 10 patients described as suffering from "arthrosis". In none of the patients in a fourth group suffering from spondylosis, however, has any improvement been observed. No serious toxic effects were noted, and patients tolerated the preparation very well, though 12 patients had some gastric disturbance and loss of appetite and 2 mild diarrhoea, 2 developed rashes, and 9 complained of tiredness. After temporarily reducing the dosage in these cases the original dose could be resumed. *Robert Hodgkinson*

1090. **The Collagen Fibrillar Structure of the Articular Cartilage of the Knees Studied with the Aid of Polarized Light.** (Estructuración fibrilar colágena del cartílago articular de la rodilla, con la ayuda de la luz polarizada)
M. GUIRAO PÉREZ. *Revista española de reumatismo y enfermedades osteoarticulares* [*Rev. esp. Reum.*] **5**, 278–304, Jan., 1954 (received June, 1954). 19 figs.

The author describes an investigation at the Karolinska Institute, Stockholm, into the disposition and direction of the collagen fibres in the articular cartilage of the knee-joint, the material consisting of 34 fresh post-mortem foetal and adult joints. His method consists in filling the cavities with indian ink and observing prepared sections by means of polarized light. The technique is given in detail. He describes five zones of fibres—vertical, oblique, horizontal, perpendicular, and superficial—and attempts to relate their direction to the mechanical function of the joint. His conclusions are supported and illustrated by photomicrographs, diagrams, and drawings, and the literature is discussed in detail at considerable length. *L. Michaelis*

RHEUMATIC FEVER

1091. **The Prothrombin Time in Rheumatic Fever.** (Le temps de prothrombine dans le rhumatisme articulaire aigu)
J. STERNE. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **47**, 257–262, March, 1954.

This study, carried out on 54 cases at the Maurice Gaud Hospital, Casablanca, is claimed to be the first systematic investigation of the changes in prothrombin time in rheumatic fever. All samples were collected by the same observer and estimations were made by Quick's method. The results were divided into three categories: (I) normal, when the reading was 80% or above; (II) moderately lowered (50 to 75%); and (III) considerably lowered, when the figure was 50% of normal or below. Of the 54 patients investigated, 12 belonged to Category I, 19 to Category II, and 23 to Category III. Of 15 patients without cardiac involvement, the prothrombin time was normal in 6, reduced in 3, and low in 6, but in the 39 patients with cardiac involvement it was normal in only 6, reduced in 16, and considerably lowered in 17.

Prothrombin time and erythrocyte sedimentation rate (E.S.R.) do not necessarily run parallel; a reduction in the former was found to be the better guide to a coming relapse in a number of cases. An accelerated E.S.R. may coexist with a normal prothrombin time, but the latter may be 50% of normal while the E.S.R. is 3 to 10 mm. in the first hour (Westergren). The value of prothrombin time estimation is greater than that of the E.S.R. in that it is more specific in acute arthritis. Prothrombin time is decreased in rheumatic fever, but not in rheumatoid arthritis, and thus has diagnostic importance; the only other type of arthritis in which it is decreased is acute gonococcal arthritis. In spite of the decreased prothrombin time in rheumatic fever there is marked tolerance to heparin, and this also is said to be of diagnostic significance. *D. Preiskel*

1092. **Active Rheumatic Heart Disease in Patients over Sixty**
J. W. GRIFONE and J. R. KITCHELL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **154**, 1341–1343, April 17, 1954. 7 refs.

It is pointed out that acute rheumatic heart disease is usually seen only in children or young adults, and is not often diagnosed in patients over 60 years of age. In this paper 4 cases are reported from the Presbyterian Hospital, Philadelphia, in which the patients, all over 60

years, were thought to be suffering from rheumatic heart disease. One woman aged 62 years, who had had hypertension for 11 years, developed fever and tachycardia; the electrocardiogram showed evidence of left bundle-branch block. She died after 27 days in hospital, and necropsy revealed thickening and contraction of the mitral valve and chordae tendineae and Aschoff nodes in the myocardium. A man of 76 years with a history of pain and stiffness in the joints of 2 years' duration was admitted with fever, tachycardia, and pain in the left side of his chest. He died from bronchopneumonia, and at necropsy rheumatic pancarditis was found. In the remaining 2 cases, in females aged 74 and 68 years respectively, fever, tachycardia, and apical systolic murmurs were present on admission. The fever did not respond to treatment with antibiotics, but after administration of salicylates the temperature promptly became normal. One of these patients remained well for 2½ years, but the other subsequently required treatment for mild congestive cardiac failure. The authors consider that both patients had rheumatic carditis, though the diagnosis was not certain. *C. E. Quin*

1093. **Comparative Effects of Aspirin, ACTH and Cortisone on the Acute Course of Rheumatic Fever in Young Adult Males**

H. B. Houser, E. J. Clark, and B. L. Stolzer. *American Journal of Medicine* [*Amer. J. Med.*] **16**, 168–180, Feb., 1954. 7 figs., 15 refs.

The comparative efficacy of aspirin, cortisone, and ACTH in the treatment of acute rheumatic fever was investigated at the United States Air Force Hospital, Wyoming. Of 148 young adult males with acute rheumatic fever admitted between January, 1951, and June, 1952, 61 received aspirin, 45 cortisone, and 42 ACTH. Full details are given of the diagnostic criteria, the investigations carried out, and the dosage of the drugs.

The results showed that fever and joint pain subsided more rapidly in the patients given aspirin than in those given cortisone or ACTH, but that otherwise there was little difference between the three drugs in their effect on symptoms. Relapse after the cessation of treatment occurred in most cases in all three groups. The authors state that the effect of the drugs on rheumatic carditis cannot be determined until the results of a long-term follow-up are known, but in each group there were cases in which new murmurs were elicited, these persisting while the patient was receiving a full therapeutic dose of the drug.

It is concluded that none of these three drugs is ideal for the treatment of acute rheumatism; indeed, in the authors' view no adequate treatment for this disease is yet available. *Kathleen M. Lawther*

1094. **The Treatment of Rheumatic Fever with PAS and with a Combination of PAS and Sodium Salicylate.** (Sul trattamento della infezione reumatica con PAS e con l'associazione PAS-salicilato di sodio)

R. Bulgarelli and G. Sardini. *Minerva pediatrica* [*Minerva pediat. (Torino)*] **6**, 198–201, March 31, 1954. 3 figs.

CHRONIC RHEUMATISM

1095. **Intraarticular Hydrocortisone Acetate in Rheumatic Disorders**

J. Bornstein, M. Silver, D. H. Neustadt, S. Berkowitz, and O. Steinbrocker. *Geriatrics* [*Geriatrics*] **9**, 205–210, May, 1954. 7 refs.

In this paper from the Lenox Hill Hospital and the Hospital for Joint Diseases, New York City, are recorded the results, in 88 patients with rheumatic disorders, of giving a total of 280 local injections of hydrocortisone acetate. Their ages ranged from 5 to 75 years, the largest number being in the 4th, 5th, and 6th decades. Of the 88 patients, 35 had rheumatoid arthritis and 25 osteoarthritis; the remainder had miscellaneous conditions. The dose was 1 or 2 ml. [*sic*] at intervals varying from a few days to several weeks, according to the rate of return of symptoms.

The results were good in rheumatoid arthritis, 83% of the joints injected showing some benefit. In osteoarthritis improvement was obtained only in 48%, and was purely subjective in the majority of these. Especially good responses were observed in the 7 cases of tenosynovitis of the fingers, 5 showing complete resolution and the other 2 " major improvement ". Four out of 5 patients with acute calcific tendinitis also benefited greatly after injections into the supraspinatus tendon. The duration of effect was very variable, but in the majority of cases reinjection was needed at intervals of 1 to 2 weeks.

The authors consider that one of the chief advantages of local hydrocortisone therapy is avoidance of systemic hormonal effects, especially in patients with rheumatoid arthritis and osteoarthritis, who tend to belong to the older age groups in which there is a liability to such complications as heart failure, mental disturbances, and pathological fractures. *K. C. Robinson*

1096. **Syndromes of Rheumatoid Arthritis**

G. D. Kersley. *Lancet* [*Lancet*] **1**, 1206–1209, June 12, 1954. 5 figs., 21 refs.

From a wide clinical experience the author discusses, with case records, four syndromes in rheumatoid arthritis in which the differential diagnosis is based upon the mode of onset of the disease. These four syndromes are neither frequent nor a usual feature of the classic disease process —the author found one or other of them in only 67 out of a recent series of 750 cases of rheumatoid arthritis— but they are none the less distinct and individual. In 38 of the 750 cases the onset was so acute as to resemble that of rheumatic fever, but only one patient actually developed carditis. The differential diagnosis, which is discussed, is helped by the therapeutic response to colchicine, antibiotics, and salicylates. [The classification of this first group as " acute arthritis " closely resembles a major subdivision recognized in Scandinavia, in which cases of rheumatoid arthritis are divided into two groups —those with " acute " and those with " chronic " onset. The number of acute cases in this series would seem by comparison to be relatively small.] In a second group

of 11 cases there was involvement of only one joint initially, and in 2 of these cases there was evidence of a tuberculous focus in the synovium, despite the close histological resemblance to rheumatoid arthritis. It is suggested that when tuberculous and rheumatoid foci appear in the same joint the " rheumatoid " reaction may be due to a non-specific reaction of the joint to sensitization to tuberculous infection. In a third group of 13 cases the onset of rheumatoid arthritis was episodic, and here the differential diagnosis was from gout, palindromic rheumatism, angioneural arthrosis, allergic arthritis, and intermittent hydrarthrosis. In a fourth group of 5 cases rheumatoid arthritis had progressed for a number of years without pain. There was gross destruction of bone and joint, but no evidence of neurological disease. Variation in the general threshold to pain and rheumatoid lesions of the perineurium were not considered to play any part. *Harry Coke*

1097. **The Systemic Lesions of Malignant Rheumatoid Arthritis**

M. BEVANS, J. NADELL, F. DEMARTINI, and C. RAGAN. *American Journal of Medicine* [*Amer. J. Med.*] **16**, 197–211, Feb., 1954. 18 figs., 12 refs.

Although the incidence of rheumatic heart disease is said to be higher in patients with rheumatoid arthritis than in the general hospital population, there is evidence that valvulitis and other stigmata of rheumatic heart disease are infrequent in those suffering from rheumatoid arthritis except when a straightforward history of rheumatic fever can be obtained. In this paper from Columbia University, New York, is described a study of 2 cases of active rheumatoid arthritis complicated clinically by pleurisy and pericarditis. The duration of the rheumatoid arthritis was 10 and 16 years respectively. In the first case there were intercurrent diabetes and renal papillary necrosis, and the second patient also had epilepsy. Long-term treatment with cortisone and corticotrophin did not appear to arrest the course of the disease, and compression fractures occurred in both cases as a result of osteoporosis arising during the hormone therapy. Both patients died.

At necropsy an inflammatory obliteration of pleural and pericardial sacs was seen, together with lesions in the myocardium and valve rings due to granulomata appearing " indistinguishable from the subcutaneous nodules of rheumatic disease ". In the first case similar lesions were also found in the kidney, and in the second case in the lungs. Both patients had oesophagitis and episcleritis. The authors consider that the granulomatous lesions develop from fibrinoid necrosis of the vessel wall.

Evidence is adduced that there exists a malignant form of rheumatoid arthritis, of which the 2 cases described are regarded as examples. The relationship of this fulminating disease to the reputed high incidence of rheumatic heart disease in patients with rheumatoid arthritis is discussed. It is concluded that long-term cortisone therapy apparently does not prevent the development of this form of rheumatoid arthritis.

E. G. L. Bywaters

1098. **Management of Rheumatoid Arthritis with Prolonged Cortisone Administration**

W. S. C. COPEMAN, O. SAVAGE, C. DODDS, J. H. GLYN, and M. E. FEARNLEY. *British Medical Journal* [*Brit. med. J.*] **1**, 1109–1113, May 15, 1954. 1 fig., 11 refs.

The results are presented of 20 cases of rheumatoid arthritis treated with cortisone at the West London Hospital, Hammersmith, 14 of which received the drug for more than 2 years and all for at least a year continuously. All 20 cases were severe, and none of the patients was able to follow his or her normal occupation. The usual methods of treatment had been tried without halting the progress of the disease. The average maintenance dose of cortisone by the oral route was 69 mg. a day, varying in individual cases from 37·5 to 100 mg. daily. No fewer than 17 of the 20 patients improved sufficiently with this treatment to return to work.

Administration of the drug had to be stopped in 2 cases, in one of which severe depression occurred, and in the other the blood pressure rose from 120/80 to 200/105 mm. Hg. In 3 cases gastrointestinal complications (duodenal ulceration, oesophagitis associated with hiatus hernia, and melaena respectively) developed, but it was not found necessary to discontinue treatment. Various less important side-effects were also observed.

The authors conclude that cortisone is a practical addition to treatment in selected cases of rheumatoid arthritis, but they emphasize that careful and constant supervision is necessary. *K. C. Robinson*

1099. **Observations on the Antirheumatic and Physiologic Effects of Phenylbutazone (Butazolidin) and Some Comparisons with Cortisone**

B. B. BRODIE, E. W. LOWMAN, J. J. BURNS, P. R. LEE, T. CHENKIN, A. GOLDMAN, M. WEINER, and J. M. STEELE. *American Journal of Medicine* [*Amer. J. Med.*] **16**, 181–190, Feb., 1954. 5 figs., 22 refs.

Phenylbutazone was given to 18 patients severely disabled with rheumatoid arthritis and to 69 non-arthritic rheumatic patients. It is pointed out that the plasma concentration of phenylbutazone does not increase commensurately with an increase in the dose, but tends to approach a limit; the peak level with a daily dose of 1,600 mg. is not appreciably higher than that achieved with a daily dose of 800 mg. In the present investigation, therefore, each patient was given 800 mg. by mouth daily; later, some of the patients were given cortisone for comparison. A major improvement was noted in 8 of the patients with arthritis, but minor improvement only in the others. The results obtained with cortisone were similar. Side-effects were severe enough in 17 of the 87 patients to call for cessation of treatment, but in none of the cases did agranulocytosis develop.

Phenylbutazone caused urinary retention of sodium, chloride, and water, but did not affect potassium or 17-ketosteroid excretion; in none of the cases was significant eosinopenia found. The fall in the erythrocyte count and haemoglobin level during treatment was due to haemodilution and not to depression of haematopoiesis. From their observations the authors conclude that the drug does not act through stimulation of the adrenal

cortex. They consider that its anti-rheumatic effect is similar to that of cortisone and ACTH, but that there is no risk of hormonal imbalance with phenylbutazone. It is hoped that these encouraging clinical results will stimulate further search for other non-steroid drugs exerting " a desirable local tissue effect ".

Kathleen M. Lawther

1100. **A New Form of Drug Therapy in the Treatment of Arthritis and Rheumatoid Conditions**

A. L. NATENSHON. *Wisconsin Medical Journal* [*Wis. med. J.*] **53**, 223–225, April, 1954. 5 refs.

The author has treated 200 unselected patients of various ages suffering from " arthritis in any form, acute or chronic; myositis; or any painful muscle condition, regardless of the cause " with " salimeph-C ", a preparation containing 250 mg. of salicylamide, 250 mg. of mephenesin, and 15 mg. of ascorbic acid in each tablet. It is stated that this combination is effective because mephenesin relaxes muscle spasm, salicylamide relieves pain without causing gastric irritation, and ascorbic acid compensates for depletion of vitamin C caused by salicylate.

Two tablets of salimeph-C were given 3 or 4 times a day after meals initially, to which dosage most patients responded within 3 days with loss of pain and stiffness and could then be kept symptom-free on 1 or 2 tablets daily. There were no side-effects, and it is claimed that results were " extremely good " in nearly all the patients, many who had been bedridden being able to get about without assistance. The treatment was effective in traumatic conditions (in which, however, other forms of treatment were also given), but did not relieve pain due to prolapse of an intervertebral disk or to calcified bursitis.

[There is no report of a control series, and no objective method of assessing improvement appears to have been used.] *F. Clifford Rose*

See also Physical Medicine, Abstract 1105.

GOUT

1101. **Phenylbutazone (Butazolidin) in Gout**

W. C. KUZELL, R. W. SCHAFFARZICK, W. E. NAUGLER, G. GAUDIN, E. A. MANKLE, and B. BROWN. *American Journal of Medicine* [*Amer. J. Med.*] **16**, 212–217, Feb., 1954. 4 figs., 13 refs.

In an attempt to evaluate the therapeutic efficacy of phenylbutazone 200 patients (156 males and 44 postmenopausal females) suffering from acute gout and/or chronic gouty arthritis and treated with this drug were studied at Stanford University School of Medicine, San Francisco, in the 30 months November, 1950, to May, 1953. During the first 8 months " irgapyrin " (containing equal parts of phenylbutazone and amidopyrine) was used. For the most part phenylbutazone was given orally; when injected intramuscularly it was given in the form of its sodium salt (20% solution) and occasionally combined with a local analgesic. A series of 408 cases of musculo-skeletal disorders other than gout, also treated with phenylbutazone, were used as controls, the serum uric acid level being estimated before and after treatment.

In acute gout an injection of 1 mg. of phenylbutazone daily for 1 to 3 days sufficed to relieve symptoms. The extent of such relief was greater than that previously experienced with colchicine and/or hormone therapy, and was occasionally noted in less than one hour. Small oral doses (200 to 400 mg. daily) also caused rapid subsidence of symptoms. The attack rate among patients receiving a small daily dose (200 to 600 mg.) was greatly reduced. Those with acute gout responded better than those with chronic gouty arthritis, and in general males did better than females. The serum uric acid level in those receiving a maintenance dose of 100 mg. daily did not appear to be decreased, but the " uric acid pool " was not estimated; tophi were not influenced in any way. Toxic effects were slight and necessitated discontinuation of treatment in 7% of gouty cases; of the non-gouty patients the drug had to be stopped in 22%. It was also noted that the relief of pain in the non-gouty group was less in patients with a raised serum uric acid level than in those in which it was normal, this suggesting that the characteristic lowering of serum uric acid level by phenylbutazone was not the most important pharmacological action of the drug.

Though phenylbutazone appears to have a specific effect in gout, its mode of action has still to be determined. The authors have been unable to confirm the alleged increased urinary excretion of uric acid, and they explain how errors in calculation are apt to arise. Possibly, they state, the drug acts by delaying the degradation of nuclein; it may also affect enzymes concerned in the metabolism of purines. In a concentration of 1:5,000 phenylbutazone will completely inhibit the growth of yeast, and this inhibition seems to be unaffected by the addition of a variety of substances, such as ascorbic acid, glucose, and vitamin-B complex. On the other hand, sodium bicarbonate in a concentration of 1:1,000 decreases this inhibitory effect by 70%.

D. Preiskel

1102. **The Effect of Intravenous Colchicine on Acute Gout**

J. S. DAVIS and H. BARTFELD. *American Journal of Medicine* [*Amer. J. Med.*] **16**, 218–219, Feb., 1954.

In the past the authors have often treated acute gout by injecting intravenously the contents of a 20-ml. ampoule containing 0·65 mg. colchicine, 1 g. sodium salicylate, and 1 g. sodium iodide. Side-effects, such as intestinal haemorrhage, were not uncommon. As these were ascribed to salicylates and iodides, the authors, in an investigation at St. Luke's Hospital, New York, decided to omit these substances and prepare a solution containing 0·65 mg. (1/100 gr.) of colchicine in distilled water in 1- and 2-ml. ampoules. This modified preparation was given to 16 patients suffering from acute attacks of gout. In some cases up to 8 injections were required to bring the attack under complete control, but in 4 instances the attack was aborted by a single injection, pain and swelling often beginning to subside within 5 to 15 minutes. *D. Preiskel*

Physical Medicine

1103. **Center of Gravity Line in Relation to Ankle Joint in Erect Standing. Application to Posture Training and to Artificial Legs**
S. BRUNNSTROM. *Physical Therapy Review* [*Phys. Ther. Rev.*] **34**, 109–115, March, 1954. 2 figs., 22 refs.

It has been widely accepted that in a good standing posture, viewed laterally, a vertical line passes through the tip of the ear, the acromion process, and the hip-, knee-, and ankle-joints, the centre of gravity being on this line. In this paper from the Kessler Institute of Rehabilitation, West Orange, New Jersey, evidence is presented to disprove this.

Braune and Fischer in 1889 studied posture and determined the centre of gravity by mechanical methods on frozen cadavers. They formulated the present accepted standard, but stated that in a " comfortable " posture or a " military " posture, the centre of gravity passed in front of the ankle-joint. It is suggested that the present standards of posture are based on a misinterpretation of the original work on cadavers. Hellebrant investigated the centre of gravity in living subjects and also the antero-posterior oscillations in the erect position. In the present author's view this work suggests that there is an automatic neuromuscular mechanism which tends to equilibrate the body to maintain stability.

The evidence presented indicates that the vertical projection of the centre of gravity passes anteriorly to the ankle-joint. The importance of this conception in relation to artificial limbs and posture training is discussed.

J. B. Millard

1104. **Rehabilitation of Hands Injured in Industrial Accidents**
B. CLAS. *Physical Therapy Review* [*Phys. Ther. Rev.*] 34, 115–118, March, 1954. 4 figs.

Of an average of 247 patients treated daily at the Puerto Rican State Insurance Fund Rehabilitation Center, Santurce, 29% had tendon injuries of the hand. In most cases the injury was to the extensor tendons of the left hand, which the patient had sustained while cutting sugar cane. The present author describes his technique of treatment as follows. An end-to-end suture of the tendon with a pull-out wire is performed and the hand immobilized in plaster of Paris. To prevent post-operative oedema the arm is elevated for 48 to 72 hours, after which general exercises and active movement to the unaffected elbow and shoulder are started. After 3 weeks the plaster and sutures are removed, and active, passive, and progressive-resistance exercises, together with the remedial games, are begun. A faradic current is applied to the affected muscles, and various forms of heat—including infra-red rays and whirlpool—and massage are given to improve the circulation and to reduce oedema; gentle passive movements are instituted so that adhesions are stretched and eventually loosened.

Progressive-resistance exercises, based on the Oxford technique, are given by means of a simple and effective apparatus. This consists of two vertical parallel bars, one of which is fixed, which are gripped between the thumb and fingers. The mobile bar, under the fingers, is connected by a pulley system to a lever carrying a movable weight, and the resistance is adjusted by moving the weight on the lever. Starting with the highest tolerated resistance, ten grips are made at a constantly decreasing level of weight load. This exercise is performed daily and the initial load is increased each week. When the patient can lift a certain weight functional tests are carried out to determine his ability to return to his previous occupation.

J. B. Millard

1105. **Citrate Iontophoresis in Rheumatoid Arthritis of the Hands**
A. B. COYER. *Annals of Physical Medicine* [*Ann. phys. Med.*] **2**, 16–19, Jan., 1954. 1 fig., 7 refs.

Following the observations of Rocha e Silva (*Brit. med. J.*, 1952, **1**, 779) on the value of citrate in allergic and anaphylactic reactions, the present author, at St. Thomas's Hospital, London, used citrate iontophoresis in cases of acute rheumatoid arthritis of the hands on the grounds that the rheumatoid process is, in part, an allergic process. He produces evidence to show that citrate may reasonably be expected to reach the affected tissues when given in this way.

One group of 15 patients received citrate ionization, a second group of 10 patients received anodal galvanism, and a third group, also of 10 patients, received cathodal galvanism; the last two groups served as controls. The citrate iontophoresis was given in a cathodal bath containing 2% potassium citrate solution, a current of about 10 mA being passed for 20 to 30 minutes. In the control cases the bath contained tap-water. Patients were treated on alternate days for 4 weeks, and the results were assessed weekly, mainly by determining the strength of grip in the hand.

There was a much greater improvement in strength of grip in those patients treated with citrate than in the control groups. The author notes that some of the patients had previously failed to respond to more conventional methods of physiotherapy, such as wax baths and local application of heat, but that these patients tended to have a relapse when treatment ceased.

B. E. W. Mace

1106. **The Effect of Infra-red Irradiation of the Hand on Manual Skill at Various Room Temperatures.** (Über den Einfluss von Wärmebestrahlung der Hand auf die Handgeschicklichkeit bei verschiedener Zimmertemperatur)
K. VETTER. *Arbeitsphysiologie* [*Arbeitsphysiologie*] **15**, 273–276, 1954. 3 figs., 3 refs.

Neurology and Neurosurgery

1107. **A Note on the Reliability of Electroencephalographic Judgments**
R. H. BLUM. *Neurology* [*Neurology*] **4**, 143–146, Feb., 1954. 9 refs.

In this limited study, carried out at Stanford University, California, and designed to test the reliability of interpretation of electroencephalographic (EEG) records, the electroencephalograms of 10 subjects were examined by 5 different neurologists, all practised in the interpretation of such records. They were asked to state whether the EEG was normal, borderline, or abnormal, and whether it showed local or generalized disturbance.

The percentage of complete agreement on abnormality was 40, on localization 30, and on both combined only 10. This evidence of inconsistency in interpretation as between the different examiners is, as Aird (who was asked to comment on these results) points out, not so much a test of the validity of electroencephalography as of the homogeneity of the training of the different electroencephalographers who made the records. The only true test, Aird adds, would be to compare the results of electroencephalography with the known facts as established by other methods, pathological or clinical. The author insists, however, that the whole question of the reliability of EEG interpretation requires further and more detailed investigation. *J. Foley*

1108. **A Contribution to the Study of the Progressive Muscular Atrophies and their Electromyographic Diagnosis.** (Contribution à l'étude des atrophies musculaires progressives. Leur diagnostic électromyographique)
F. THIÉBAUT, F. ISCH, and C. ISCH-TREUSSARD. *Revue neurologique* [*Rev. neurol.* (*Paris*)] **89**, 333–355, 1953. [received April, 1954]. 10 figs., 9 refs.

The value of electromyography in the differential diagnosis of various types of muscular atrophy has become widely recognized. In the study here reported from the Neurological Clinic, Faculty of Medicine, Strasbourg, electromyograms were obtained from 73 patients with progressive muscle wasting. In 39 cases the atrophy was neurogenic, including examples of syringomyelia, lower motor neurone disease, syphilitic amyotrophy, progressive spinal muscular atrophy, peroneal muscular atrophy, and hypertrophic interstitial neuritis; the remaining 34 patients suffered from primary muscle disorders, mostly progressive muscular dystrophies but including 4 examples of dystrophia myotonica and one of dermatomyositis. Insertion electrodes were used. The presence or absence of fibrillation and fasciculation was noted, and in each muscle a recording was made during passive stretch, voluntary movement, maximal contraction, and slight contraction.

The authors conclude that in cases of progressive neurogenic atrophy the relative paucity of fibrillation potentials makes them a less important diagnostic feature than in cases of acute affections. Fasciculation, on the other hand, was commonly present in these cases and was sometimes polyphasic in character. A reaction to stretch was sometimes obtained, but its significance is obscure. An increased frequency of discharge during voluntary movement was not found to be of great diagnostic value. In most cases the duration and amplitude of the potentials were increased and the form of the potentials was often polyphasic. There was no constant relationship between the amount of muscle wasting and the electromyographic changes. The latter, moreover, have sometimes been found in healthy muscles.

In myogenic atrophy, pseudo-interference patterns were very characteristic, but occurred infrequently. It was found difficult to establish norms for voluntary and maximal effort, and analysis of the character of the motor unit was thought to be more valuable. Brief duration of the potentials was an important sign, but was also inconstant. Other things being equal, the amplitude of the potentials in myogenic atrophy was always less than in neurogenic atrophy, and the tracing also had a more jagged appearance. Apart from dystrophia myotonica, none of the so-called types of myopathy show any specific electromyographic features. The question of synchronization was investigated, but no conclusion could be reached as to whether true synchronization occurs or whether the two needles are recording from the same motor unit. *L. G. Kiloh*

1109. **Digitalgia Paresthetica and Gonyalgia Paresthetica**
R. WARTENBERG. *Neurology* [*Neurology*] **4**, 106–115, Feb., 1954. 2 figs., 13 refs.

The conditions known as digitalgia paraesthetica and gonyalgia paraesthetica are generally mild and, like meralgia paraesthetica, are the results of an isolated neuritis of a sensory nerve. The author, writing from the University of California, suggests that they are due to general causes, either infective or metabolic, rather than to local trauma, though occasionally trauma may in fact be responsible. Involvement of a digital nerve, which is rare, causes dysaesthesia, with or without numbness on one side of the finger; involvement of the infrapatellar branch of the saphenous nerve (the anatomy of which is discussed in some detail) causes sensory symptoms and signs below the knee. The onset of these neuralgias is insidious and symptoms are usually mild, but they may persist for years; any manœuvre which stretches the nerve, such as abduction of the finger or hand or flexion of the knee, causes a sharp pain like an electric shock. There appears to be no effective treatment. Two cases are described. *J. Foley*

1110. **Posterior Rhizotomy of the Second and Third Cervical Nerves for Occipital Pain**
W. R. CHAMBERS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 431–432, May 29, 1954. 2 refs.

1111. **An Analysis of Agnosia**
M. REINHOLD. *Neurology* [*Neurology*] **4**, 128–136, Feb., 1954. 2 figs., 8 refs.

In this discussion of the nature of agnosia the author, writing from the National Hospital, Queen Square, London, first considers gnosis. Gnosis involves perception, which she defines as " that qualitative experience of a conscious individual occurring as the result of the unconscious reception, selection, differentiation, and integration of sensory stimuli "; perception requires the active, if often unconscious, abstraction of sensory patterns, so that when these or similar patterns occur again they can be recognized. All sensations are endowed by the perceiver with spatial, temporal, and directional qualities.

Originally regarded by Freud as a difficulty in relating objects to object concepts, agnosia results from a disturbance of the processes of abstraction and of symbolic representation and, in the author's opinion, of the correct attribution of spatial, temporal, or directional qualities to sensory stimuli, although the physiological pathways of these stimuli may be intact. It is suggested that the disorders which are described as agnostic are concerned with those aspects of perception which require spontaneous, active, though not necessarily conscious, mental performance on the part of the individual. As an extreme example, inability to recognize a triangle is due to an inability to recognize specific spatial relationships and to associate them with the abstract concept of triangularity.

Visual disorientation may make it impossible to distinguish an object in three dimensions or to distinguish it from its background. The varieties of agnosia, such as visual object agnosia, visual verbal agnosia, acoustic verbal agnosia, acoustic musical agnosia, right–left agnosia, finger agnosia, autotopagnosia, and spatial agnosia are all different aspects of defective perception, in the psychological sense, and as a result of this defect the individual is unable to compare and contrast specific sensory relationships and extract from them their symbolic significance. Thus a patient with one variety of agnosia may be able to recognize an object by the aid of additional sensory information, for example, by feeling what he cannot recognize by sight, or by reading what he cannot recognize by sound; in doing this he transfers his perceptual activities into a sphere in which his ability to manipulate patterns is unimpaired. A distinction can thus be drawn between agnosia and dementia. In dementia this transference and manipulation is beyond the ability of the patient, in whom total mental function is more or less evenly disturbed. *J. Foley*

1112. **Frontal Lobe Wounds Causing Disinhibition. A Study of Six Cases**
H. F. JARVIE. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **17**, 14–32, Feb., 1954. 14 figs., 12 refs.

Although disinhibition—that is, a disturbance of the mechanism responsible for the control of behaviour in its social setting—is a feature of the syndrome following frontal-lobe injury, it is not often encountered in a relatively pure form. In the 6 cases described in the present paper, which were taken from the records of the Head Injury Bureau of the Military Hospital for Head Injuries, Oxford, disinhibition followed severe penetrating wounds involving one or both frontal lobes. The available evidence concerning the pre-traumatic personality of the patient suggested that in all the cases there had been over-inhibition. Disinhibition added nothing new to the personality; it merely revealed tendencies which were present before the injury but which were previously permitted only limited expression. Five of the 6 patients were aware of the change in their personality. Initiative and spontaneity were normal in 2; only one experienced any serious loss of feeling. In 5 of the cases there was no significant intellectual impairment, as judged by conceptual tests. The author concludes that disinhibition is a separate disturbance of function, not necessarily associated with the other changes which usually form part of the frontal-lobe syndrome. *J. Foley*

CEREBRAL TUMOURS

1113. **Speech Disturbances in Association with Parasagittal Frontal Lesions**
J. G. CHUSID, C. G. DE GUTIÉRREZ-MAHONEY, and M. P. MARGULES-LAVERGNE. *Journal of Neurosurgery* [*J. Neurosurg.*] **11**, 193–204, March, 1954. 11 figs., 22 refs.

The authors review the literature relating to speech disturbances in parasagittal lesions of the dominant hemisphere, giving compressed histories of 7 previous cases of parasagittal meningioma reported by Cushing and adding brief descriptions of 2 cases of their own seen at St. Vincent's Hospital, New York. They conclude that impairment of language function of varying types and degree and convulsive seizures associated with vocalization may occur in association with lesions of the medial surface of the frontal lobe of the dominant hemisphere. *Brodie Hughes*

1114. **Localization of Brain Tumors and Other Intracranial Lesions with Radioactive Iodinated Human Serum Albumin**
H. S. DUNBAR and B. S. RAY. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **98**, 433–436, April, 1954. 2 refs.

In an investigation at New York Hospital (Cornell University Medical School) radioactive-iodinated human serum albumin was used for locating the tumour in 100 cases in which an intracranial neoplasm was suspected. The isotope in this form was chosen because it remained longer in the blood stream than other compounds and enabled counts to be made up to 24 hours after injection. Counts were made with a scintillation counter at 36 points over the scalp. Lugol's iodine was usually administered for a few days previously to minimize the uptake of radioactive iodine by the thyroid.

An over-all accuracy of 76% was achieved by the isotope method in predicting the presence or absence of a tumour, in contrast to pneumoencephalography and pneumoventriculography, which were 100% accurate.

Of 47 cases without tumour a false positive result was obtained in 2 for no known reason; electroencephalography was inaccurate to a similar degree. Some 61% of cerebral tumours were correctly diagnosed by the isotope method; an even lower degree of accuracy was achieved by electroencephalography (50%), but air-contrast radiography was considerably more accurate (96%). Poor diagnosis was especially evident in the case of posterior-fossa tumours and pituitary tumours; 4 cases of subdural haematoma, on the other hand, were all diagnosed with ease.

According to the authors the success of isotope location of cerebral neoplasms appears to depend on the size and position of the tumour and its vascularity.

Donald McDonald

CEREBRAL VASCULAR DISORDERS

1115. **Basilar Artery Stenosis and Thrombosis**
J. L. SILVERSIDES. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **47**, 290–293, April, 1954.

The clinical picture and antecedent cerebral symptoms in 22 cases of basilar artery thrombosis seen at two Toronto hospitals are discussed. In 13 of the cases there was " the fairly typical clinical picture " of basilar artery thrombosis; in the remaining 9 the pre-thrombotic symptoms were of special interest. The clinical picture in the former group was one of sudden loss of consciousness, sometimes after brief initial symptoms such as general weakness, headache, vertigo, and dysarthria. Coma developed rapidly, and death followed in 1 to 8 days. In 6 of the 13 cases the thrombosis occurred in the upper portion of the basilar artery [the author refers to this as the " proximal portion "], and in these cases oculomotor palsy was observed. In the remaining 7 cases the lower [" distal "] portion of the basilar artery and the vertebral arteries were involved.

In the group of 9 cases in which there were recurrent premonitory symptoms before the terminal occlusion the clinical picture suggested periodic insufficiency of brain-stem blood flow. Further, in these and in the other cases basilar stenosis seemed to be an important causal factor in the terminal thrombosis. These premonitory symptoms were exceedingly varied, and included disturbance of consciousness, dysarthria and mutism, hemiplegia, crossed or uncrossed, and vertigo with or without tinnitus. Deafness was not encountered. In 3 cases epilepsy was noted and in 3 others paraesthesiae occurred. Some patients showed abnormal behaviour, varying from amnesia to paranoid reactions. *L. A. Liversedge*

1116. **Spontaneous Thrombosis of the Carotid Arteries**
S. K. SHAPIRO and W. T. PEYTON. *Neurology* [*Neurology*] **4**, 83–100, Feb., 1954. 4 figs., 19 refs.

The diagnosis of thrombosis of the internal carotid artery in the 17 cases here reported from the University of Minnesota Medical School, Minneapolis, was based on angiographic evidence in 11, on biopsy or post-mortem examination in 4, and on the absence of pulsation in the artery in 2; in 12 of the 17 cases the left internal carotid artery was involved, in 5 the right, and in 2 the common carotid artery was also involved. Ten of the patients were over 50, and 14 were male; 2 died. In 5 cases the onset was apoplectic, in 10 it consisted in a series of episodes culminating in a hemiplegia, while in 2 cases the slowly progressive course was suggestive of a cerebral tumour. Hemiparesis was the initial symptom in 9 cases, though in all 17 some motor weakness developed eventually; none of the patients had fits, and only one had headaches. Dysaesthesia was the initial symptom in only one case, but dysphasia occurred in 9 cases and mild dementia in 3. Visual disturbances, such as transient blindness, appeared early in 4 cases, late in a further 2, though in only 2 of these 6 cases was there typical primary optic atrophy.

The findings in the 11 cases examined by angiography were as follows: occlusion of the internal carotid artery at its origin, 2 cases; occlusion 1 cm. from its origin, 3 cases; irregular narrowing of the artery, 2 cases; no filling of the artery, even on open arteriography, 2 cases; no filling of the internal carotid artery, but retrograde filling of common carotid and external carotid arteries, one case; and retrograde filling of the vertebral artery, one case. From the examination of 5 specimens removed at biopsy no definite conclusion as to the pathology of the thrombosed artery could be reached. In one case there was polycythaemia; another patient died of periarteritis nodosa 8 years after the thrombosis of the internal carotid artery, but no evidence of periarteritis nodosa was found in this artery. The relevant histories of all 17 cases are given in some detail. *J. Foley*

1117. **The Pathologic Anatomy of Ruptured Cerebral Aneurysms**
G. WILSON, H. E. RIGGS, and C. RUPP. *Journal of Neurosurgery* [*J. Neurosurg.*] **11**, 128–134, March, 1954. 3 figs., 5 refs.

The authors describe the morbid anatomy in 143 cases of ruptured cerebral aneurysm with subarachnoid haemorrhage examined post mortem at Philadelphia General Hospital. Women predominated (91 to 52 men) and 31% of the patients were under 40 years of age. All the aneurysms were located on intracranial vessels above the carotid syphon and were distributed as follows: anterior cerebral and anterior communicating arteries, 48; internal carotid, 51; branches of the anterior, middle, and posterior cerebral arteries, 30; and basivertebral vessels, 14. The aneurysms originated at arterial branchings, though not necessarily at bifurcations, in 101 cases, and occurred as out-pouchings in 42. Multiple aneurysms were present in 27 cases. In addition to recent bleeding, evidence of earlier bleeding was present in most cases, and damage to the brain had occurred in 94 cases, consisting of frank haemorrhage (29 cases), clot adjacent to the aneurysmal sac (21), clot remote from sac (8), and focal haemorrhage and anaemic infarction (65). In most cases the brain damage was related to the site of the aneurysm or to the peripheral distribution of the branches of its artery of origin. In a few cases the brain damage seemed to be unrelated to site of the aneurysm, or it was bilateral. It is suggested

that other factors, particularly increasing intracranial pressure, may contribute to the circulatory disturbance in these cases.

Associated lesions of the cardiovascular system were present in over half the cases, and extracranial anomalies in 9 cases. Anomalies of the circle of Willis were present in 118 of 124 cases, and these anomalies are analysed in 114 cases and related to the site of aneurysm. Eight basic patterns in the circle of Willis were recognized, as follows: (1) normal, 10 cases; (2) hypoplasia of all vessels, 6 cases; (3) hypoplasia of the first part of one anterior cerebral artery, 47 cases; (4) hypoplasia of basilar divisional branches and origin of both posterior cerebral arteries from the carotid stem, 11 cases; (5) hypoplasia of one basilar divisional branch, 20 cases; (6) combination of lesions 3 and 5 on the same side, 15 cases; (7) combination of lesions 3 and 5 on opposite sides, 6 cases; and (8) combination of lesions 3 and 4, 5 cases.

No constant relationship was found between aneurysms at a particular site and any specific anomaly, although 85% of anterior cerebral aneurysms were associated with hypoplasia of the first part of one anterior cerebral artery. *Brodie Hughes*

1118. **Cortisone in the Immediate Therapy of Apoplectic Stroke**
H. I. Russek, B. L. Zohman, and A. S. Russek. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] 2, 216–222, April, 1954. 12 refs.

The results of administration of cortisone to 15 patients suffering from cerebrovascular occlusion (due to thrombosis in 9, embolism in 3, and haemorrhage in 3) are described. The drug was given by mouth in a dose of 300 mg. on each of the first two days after the stroke; this was then progressively reduced to a daily maintenance dose of 50 mg. in the third week. The 3 patients with cerebral haemorrhage died within 2 to 5 days, without showing any beneficial effect. In 9 of the remaining 12 patients there was "dramatic" clinical improvement within 24 to 48 hours of the start of cortisone therapy. Relapse occurred in 2 of the 3 cases in which the drug was intentionally withheld after one week, but improvement rapidly followed re-administration of cortisone. No "rebound" phenomenon was observed in the other cases when treatment ceased after 3 weeks. The authors conclude that cortisone is of value in the treatment of acute cerebral thrombosis or embolism.

P. D. Bedford

1119. **Delayed Traumatic Intracerebral Haemorrhage (*traumatische Spätapoplexie*)**
K. G. Jamieson. *Australian and New Zealand Journal of Surgery* [*Aust. N.Z. J. Surg.*] **23**, 300–307, May, 1954. 8 figs., 10 refs.

The term *traumatische Spätapoplexie* was introduced by Bollinger in 1891 to describe an intracerebral haemorrhage caused by, but occurring at some time after, a head injury. Since that date there has been considerable discussion, some authors denying its existence, while others have speculated on the possibility that minor head injuries may play a part in the aetiology of any case of cerebral haemorrhage. Well-authenticated cases are rare, and very few of those reported in the literature can be regarded as proven.

In the present paper are described 2 cases seen within a few weeks of each other at the Alfred Hospital, Sydney. One case is "as well documented as any in the literature". The other, however, lacked pathological exclusion of an alternative cause of haemorrhage such as ruptured aneurysm, but in all other respects appears to satisfy the criteria laid down by the author. Full case histories and commentaries are given. The differential diagnosis from other complications of cranial trauma and from other "spontaneous" intracerebral haemorrhages is considered and the various types of traumatic intracerebral haemorrhage briefly discussed. The pathogenesis of delayed traumatic intracerebral haemorrhage is thought by the author to be that suggested by Bollinger —that cerebral injury results in softening which involves a vessel wall. The criteria for diagnosis and for medico-legal opinion are presented. *J. V. Crawford*

EPILEPSY

1120. **Traumatic Epilepsy after Closed Head Injury**
G. Phillips. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **17**, 1–10, Feb., 1954. 1 fig., 7 refs.

The incidence and clinical features of traumatic epilepsy as seen in 2,000 cases of closed head injury at the Military Hospital for Head Injuries, Oxford, are discussed. Two groups of cases were studied in detail: (1) 500 cases admitted in the acute post-traumatic stage; and (2) all the cases (190) of post-traumatic epilepsy found in the total series of 2,000. Of the 500 patients in Group 1, 31 developed fits, the attacks being focal in 5. It is believed that the incidence of epilepsy in these 500 cases "is a reasonably accurate measure of traumatic epilepsy in a young, healthy, male population after severe head injury". The 190 cases in Group 2, on the other hand, do not represent the incidence in 2,000 cases, since many of the patients were selected for admission for treatment of the epileptic attacks.

The delay in onset of epileptic attacks in Group 2 was of special interest, there being three phases in the curve of incidence of the first fit. In the first phase the initial fit occurred within 3 months of the injury; 104 of the 190 patients had the first fit within this period, 66 of them within the first month. In most of these cases there was a single seizure and no recurrence. The number of cases in which the first fit occurred in the reactionary phase—that is, after 3 months—rapidly decreased from 27 at an interval of 3 to 6 months after injury to 2 at an interval of 15 to 18 months. There was then a period of 18 months to 2 years during which none of the patients had an epileptic attack. The author states that epilepsy beginning in the reactionary phase responded well to treatment. In a small group of 28 cases the fits started in the secondary phase—that is, after 2 years—the seizures being considered to be a

reaction to the presence of dead tissue. Epilepsy beginning in this phase was difficult to control.

Discussing this latent interval the author suggests: (1) that trauma itself is not the direct cause of the fits; and (2) that the epileptogenic factor is related to enhanced excitability of cells recovering from the effects of injury. This would explain the rapid fall in the time-lag gradient after 3 months, as there is then a rapidly diminishing number of recovering neurones from which seizures may originate. This hypothesis receives support from two facts: (1) the incidence of traumatic epilepsy is related to the severity of the closed head injury, and (2) the longer the duration of post-traumatic amnesia, by which the severity of the injury is judged, the longer is the latent period before the onset of fits—that is, in the majority of cases in which the post-traumatic amnesia is of short duration the first, and often only, fit occurs within 3 months, while in the majority of cases in which the post-traumatic amnesia is of long duration the first fit occurs after 3 months.

The available evidence suggests that a personal or family history of epilepsy does not render the patient more liable to traumatic epilepsy, and that a previous head injury does not lower the convulsive threshold. Moreover, complications such as fractured base and cerebrospinal rhinorrhoea do not materially increase the incidence of traumatic epilepsy. The exception to this is the case in which there is a depressed fracture; the incidence of epilepsy is higher and the onset is earlier in such cases, and the author suggests that anticonvulsants should be given as a routine. *J. Foley*

1121. Visceral Epilepsy

D. W. MULDER, D. DALY, and A. A. BAILEY. *Archives of Internal Medicine* [*Arch. intern. Med.*] **93**, 481–493, April, 1954. 34 refs.

The authors, at the Mayo Clinic, Rochester, Minnesota, studied the subjective visceral symptoms described by 100 epileptic patients, the symptoms occurring either as an aura of the attack or as the attack itself.

Gastrointestinal symptoms were the most frequent. Nausea, vomiting, and borborygmi were the most usual symptoms in 67 patients, and abdominal discomfort was noted by 31 of these. Symptoms referable to the cardiac and respiratory systems were also frequently encountered. Less commonly noted were sensations arising from the epigastrium and symptoms referable to the genito-urinary tract.

Of the 100 patients, 83 had a focal cerebral lesion as shown either by surgical exploration (28 patients) or by an abnormal electroencephalographic discharge (55 patients). The focus was in the temporal lobe in 75 cases, and in 5 others the frontal parasagittal region was involved. A tumour was present in 32 of these cases.

The authors note that the anatomical basis for these visceral phenomena is not entirely clear, although there is some evidence that the tip of the temporal lobe, the amygdaloid complex, and the frontal lobes project on to the ventromedial hypothalamic nuclei, stimulation of which may produce autonomic phenomena.

E. C. Hutchinson

PARALYSIS AGITANS

1122. Five Year Follow-up of Treatment with Trihexyphenidyl (Artane). Outcome in Four Hundred Eleven Cases of Paralysis Agitans

L. J. DOSHAY, K. CONSTABLE, and A. ZIER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **154**, 1334–1336, April 17, 1954. 14 refs.

The authors present a survey based on a 5-year follow-up of 411 cases of paralysis agitans treated with trihexyphenidyl at the Vanderbilt Clinic and the Neurological Institute of the Presbyterian Hospital, New York. Of these, 166 were classified as post-encephalitic, 112 as idiopathic, and 133 as arteriosclerotic. Nearly two-thirds of the patients were men. The dose of trihexyphenidyl varied from 2 to 7·5 mg. a day in the arteriosclerotic cases, from 6 to 10 mg. a day in the idiopathic cases, and from 7·5 to 30 mg. in the post-encephalitic cases. While most of the other standard remedies were given from time to time, trihexyphenidyl was used substantially alone in 60 to 70% of cases.

Treatment was continued for 5 years by 17% of the patients, for 4 years by 26%, for 3 years by 20%, for 1 to 2 years by 15%, and for less than a year by 21%. Improvement while receiving treatment was noted in 73% of the patients, in each group younger patients showing a better response than older ones. As regards side-reactions, there were 159 instances of dryness of the mouth and blurring of vision; other side-effects were nausea (24), akinesia (18), dizziness (18), and mental confusion (15).

The authors comment that " the acclaim that has been given this drug . . . is not accidental, but is directly related to its intrinsic values. . . . The fact that 182 patients, or 44% of the series, derived benefits from the drug after taking it continuously for 3 to 5 years indicates that there is no great increase in tolerance to it and that patients can continue to take it with benefit for a long time ".

[This is an unsatisfactory paper. It reads like a piece of special pleading rather than an unbiased attempt at evaluation. The fact that by the end of 5 years 83% of the patients had ceased to take the drug might suggest that they were less enthusiastic than the authors.]

N. S. Alcock

1123. Ansotomy in Paralysis Agitans

E. A. SPIEGEL and H. T. WYCIS. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **71**, 598–614, May, 1954. 10 figs., 33 refs.

The authors describe, from the Temple University School of Medicine, Philadelphia, the results obtained in the treatment of Parkinson's disease from the reduction of the pallidofugal impulses by means of lesions artificially induced in the ansa lenticularis (ansotomy). Directions are given for computation of the coordinates of the ansa; as a point of reference the anterior commissure was chosen, the position of which can be visualized by radiography after filling with air the anterior part of the 3rd ventricle and its communication

with the lateral ventricle through the foramen of Monro. The electrical discharges from the ansa were recorded by means of concentric needle electrodes, and the lesions were produced by stylet electrodes specially devised by the authors.

The operation was performed under local analgesia, so that the effect of each electrolytic lesion upon the tremor, as well as the ability of the patient to perform voluntary movements, could be observed. Two cases of idiopathic Parkinson's disease and 4 of post-encephalitic Parkinsonism are described. The results in these 6 cases were encouraging. Ansotomy caused the tremor on the opposite side to cease almost completely in 2 cases and to be much reduced in the other 4. In contradistinction to the paralysing effect of operations on the cortex and the spinal cord, these results were obtained with preservation of volitional movements, and without increase of muscle tone or disturbance of sensation.

In view of the small number of cases and the lack of histological control, the authors are reluctant to draw definite conclusions at present, particularly regarding the long-range effects and the role played by the pallidum in the mechanism of tonus innervation and in the genesis of the tremor. They feel, however, that it is possible to outline a working hypothesis regarding the mechanism of Parkinsonian tremor, basing it upon these experiences and upon animal experiments in which tegmental stimulation was combined with mesencephalic lesions. From this work it is deduced that static tremor is due to the release of the reflex arcs which serve static innervation and synapse in the rhombencephalic and mesencephalic reticulate substance—the arcs being released from inhibiting influences that originate chiefly, but not exclusively, in the substantia nigra. The experimental evidence that lesions of the ansa result in diminution or even abolition of the tremor suggests that at least some of the pallidofugal impulses have a facilitating effect upon the tremor-generating area of the reticulate substance. The role of other pallidofugal fibres is being studied.

D. P. McDonald

DISSEMINATED SCLEROSIS

1124. **The Aetiology of Retrobulbar Neuritis.** (Zur Ätiologie der Neuritis retrobulbaris)

H. ECKSTEIN. *Confinia neurologica* [*Confin. neurol. (Basel)*] **14**, 8–26, 1954. 3 refs.

In the 20-year period 1929–49, 356 cases of retrobulbar neuritis occurred among patients attending the Basle University Eye Clinic. The author has attempted to determine the cause of the condition in each of these cases, some of which have been followed up for as long as 17 years, his findings being as follows. (1) Cases of disseminated sclerosis diagnosed before the development of retrobulbar neuritis, 21 (5·9%). (2) Cases in which other signs of disseminated sclerosis were found or developed subsequently, 20 (5·6%). (3) Cases with signs and symptoms very suggestive, but not diagnostic, of disseminated sclerosis, 37 (10·4%). (4) Cases in which a cerebral tumour was found on investigation of the retrobulbar neuritis, 5 (1·4%) (4 of these showed the Foster–Kennedy syndrome). (5) Syringomyelia and other nervous disorders, 5 (1·4%). (6) Intoxications (chiefly tobacco and alcohol), 173 (48·6%). (7) Syphilis, 6 (1·7%). (8) Sinusitis, 7 (1·9%). (9) Various causes (including diabetes mellitus, nephritis, arteriosclerosis, head injury, and glaucoma), 28 (7·9%). (10) Aetiology not ascertainable, 54 (15·2%). *G. S. Crockett*

1125. **Control of Urinary Incontinence in Patients with Multiple Sclerosis**

S. R. MUELLNER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **154**, 975–977, March 20, 1954. 4 figs., 8 refs.

It is estimated that one-third of all patients with disseminated sclerosis have urinary symptoms, including frequency, nocturia, urgency, incontinence, and enuresis. The author, who has observed 85 such patients over a recent 3-year period, considers that the urinary symptoms are due to imperfect voluntary control or incoordination of the striated muscles of the pelvic floor, so that a reflex contraction of the detrusor muscle consequent on a rise in intra-abdominal pressure after effort causes micturition that cannot be controlled. He describes the management of these cases, which is based on 3 simple principles: (1) the bladder must be shielded against unnecessary stimuli; (2) detrusor hyper-irritability must be reduced to eliminate incontinence; and (3) the bladder capacity must be increased to lessen frequency and nocturia. A review of the patient's activities during a typical day generally reveals any likely cause of precipitate micturition, and a way of life is then devised in which such activities are avoided. The importance of treating cystitis, if present, is emphasized. The hyperirritability of the bladder is reduced by administration of an anticholinergic drug, usually atropine sulphate; a 0·4-mg. tablet of atropine sulphate abolishes vesical irritability for 2 to 4 hours, and can be taken as indicated by the patient's own experience. If, however, atropine causes intolerable side-effects " bellafoline " or " octin " (methyl*iso*actenylamine) is given. Methantheline has not been found to be a satisfactory drug for this purpose. An indwelling catheter is used only in the most severe stages of the disease when there is an atonic bladder with overflow incontinence. *Donald McDonald*

CRANIAL NERVES

1126. **Post-traumatic Vertigo with Special Reference to Positional Nystagmus**

N. GORDON. *Lancet* [*Lancet*] **1**, 1216–1218, June 12, 1954. 1 fig., 8 refs.

Among the many patients who complain of giddiness after head injury a small minority have a true vertigo with illusions of movement. The condition is easily overlooked, and when examining patients with these symptoms, therefore, it is wise to include tests for positional nystagmus. The condition was originally described by Bárány in 1921, who showed that the nystagmus and associated vertigo are due to the position of the head

in space and not to its movement. In reviewing a number of such cases Dix and Hallpike argued that the lesion is limited to the labyrinth and suggested the name " benign positional nystagmus of paroxysmal type ".

The present author reports 5 cases seen at the National Hospital, Queen Square, London, in recent years. The nystagmus arising after trauma presents almost exactly the same clinical picture as that arising spontaneously. The patient complains of giddiness when he takes up certain postures, such as bending down to the left or putting the head back. To bring this out at examination the patient, sitting near the end of the couch with his head turned to one side, is brought back slowly over the end of the couch while he gazes at the examiner's finger. If this does not cause an attack of giddiness, the manœuvre should be repeated with the head turned to the opposite side. When the test is positive, the nystagmus and associated vertigo come on at once or within a few seconds. The patient then shows obvious signs of discomfort and, unless he can be reassured, will shut his eyes and try to sit up. However, if he can be persuaded to remain in the supine position the nystagmus, which is usually rotatory and directed towards the lower ear, will increase in rapidity and then die away, the whole cycle lasting less than half a minute; at the same time the vertigo will cease and the patient will be content to remain in that particular position for as long as required. When he sits up again, however, a briefer and less severe attack of nystagmus and vertigo may result. If the test is repeated at once, the response is often much less marked, or absent.

[This paper is worthy of notice, as this condition is not perhaps generally very well known and these cases can be quite confusing if the true aetiology is not recognized.] *N. S. Alcock*

SPINAL CORD

1127. **Pain in Paraplegia. Clinical Management and Surgical Treatment**

E. H. Botterell, J. C. Callaghan, and A. T. Jousse. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **47**, 281–288, April, 1954. 1 fig., 14 refs.

The authors point out that following spinal-cord injury pain frequently occurs in the portion of the body rendered anaesthetic. They have made a study of such pain in a group of 125 patients with traumatic paraplegia treated in the Department of Veterans Affairs Neurological Unit, Toronto, Canada. They note that the patient's assessment of the severity of his pain depends upon a number of factors, including his general state of health, intelligence, and emotional stability, though in a patient who suffers severely the anxiety, irritability, and weariness, with inability to sleep and eat, clearly indicate that his resources have been exhausted and that surgical measures to relieve pain are indicated. Cutaneous pain varies in quality and can be more or less readily located, whereas deeper pain is more diffuse, continuous, and of unchanging quality, and can be located only with difficulty.

The pain in the cases described was referred either to the dermatome corresponding to the injured segment of the cord or to the anaesthetic area below it, and pain in the trunk and lower limbs was common with lesions at all levels. The incidence of the symptom was high, since 118 patients (94%) complained of it. However, less than one-third of the group found the pain of troublesome severity, and in only 9 cases was surgery for its relief required. Severe pain was uncommon in cervical-cord injury; it was more common, however, in lesions of the thoracic cord and complete lesions of the conus and cauda equina, being most common with partial lesions at these last two levels.

The study revealed that at times the pain develops immediately at the moment of wounding or upon recovery of consciousness, but its onset may be delayed —sometimes for years. The patient's state of well-being —physical and mental—affects the severity of the symptoms, the impact of pain being greater in patients with domestic anxieties, inadequate control of micturition and defaecation, or pressure sores. Certain local conditions, such as bladder spasms and distension and faecal impaction, aggravate the pains for no demonstrable reason. A damp climate and cigarette-smoking aggravated the pain in some of the patients.

Many patients' pain is benefited by mild analgesics and a course of rehabilitation which gives hope of life outside of hospital, though time alone does not bring spontaneous relief. In the 9 patients operated upon the pain was of such severity as to demand surgical treatment in order that they might be able to start towards the goal of rehabilitation or because, having achieved this, they were forced to return to hospital. In 6 of these cases bilateral upper dorsal spinothalamic tractotomy was carried out. In 3 the result was excellent, in one good, and in one fair, and there was one failure. In one case transection of the cord and section of the posterior nerve roots at the level of injury was carried out with considerable benefit. In one case unilateral spinothalamic tractotomy was performed on three occasions, but pain continued in the analgesic area. In one patient bilateral prefrontal leucotomy produced a good result.

The authors briefly discuss the mechanism of pain in these cases. In cases of nerve-root involvement at the level of the spinal-cord injury they state that the cause of girdle pain is clear. They believe that in complete lesions of the cord pain results from disturbance of function of the nervous system central to the lesion and independent of stimuli arising below the level of injury. Possibly an escape of thalamic function results from the loss of an inhibitory effect of normal afferent impulses. In cases of incomplete cord lesions repetitive stimulation of the pain pathway may occur and may activate a neuronal pool in the reticular connexions or thalamus, causing pain.

[This study provides valuable data concerning the incidence, severity, and treatment of pain in traumatic paraplegia.] *J. E. A. O'Connell*

1128. **Spondylosis. The Known and the Unknown**

Russell Brain. *Lancet* [*Lancet*] **1**, 687–693, April 3, 1954. 9 figs., 13 refs.

Psychiatry

1129. **Psychopathic States and Attempted Suicide**
I. R. C. BATCHELOR. *British Medical Journal* [*Brit. med. J.*] **1**, 1342–1347, June 12, 1954. 7 refs.

An investigation was made into the psychiatric and social histories of 42 patients (25 men and 17 women) with a diagnosis of psychopathic state among a series of 200 consecutive cases of attempted suicide admitted to the Edinburgh Royal Infirmary during the period 1950–2. The family histories showed that there was a "broken home" in 31 of these cases, but the author was unable to conclude from this small number whether distortion or absence of parental influences is the more traumatic, nor which parent may be the more essential.

Most of the patients were aggressive, though some were quiet and evasive. Impulsiveness and unreliability were characteristic. The majority were sexually maladjusted, and many were alcoholics. Their social status generally was low and deteriorating. Nearly one-third reported absence of nervous symptoms shortly before the attempt, and 23 gave no warning of suicidal intention. The close relationship between suicidal and homicidal tendencies was evidenced by threat or actual attack in 13 cases.

In 26 (62%) of the cases the attempt was impulsive, and among the great majority the immediate stimulus was a personal quarrel, with threat of retribution as the secondary cause. Poisoning, usually by barbiturates or aspirin, was the means chosen by 38 (90%). Of motives behind the attempt, the commonest was hatred, and the next commonest the need to escape. Other motives included identification of the self with a dead relative or other person or the romantic assertion of self. In a small number the motive was the desire to change other people. Fear was not a common cause, and in only one case was guilt a factor.

Of the 42 patients, 35 were discharged from hospital within 2 weeks, 16 of these attending for further outpatient treatment. Another 6 patients (3 men and 3 women) were transferred to a mental hospital, but only one of these was certified. *E. H. Johnson*

1130. **The Living Out of "Future" Experiences under Hypnosis**
R. RUBENSTEIN and R. NEWMAN. *Science* [*Science*] **119**, 472–473, April 9, 1954. 4 figs.

The ability of the hypnotized subject to remember and re-enact specific incidents in his past life—even in his infancy—which in ordinary circumstances he is unable to remember has hitherto been widely accepted as genuine. The present authors describe an experiment on a group of 5 easily hypnotized subjects who were able, when this was suggested under hypnosis, to live out with dramatic verisimilitude events not only in their past but also in their future lives which were well within the bounds of possibility. On the assumption that these "events" were the product of the patient's imagination, it is contended that these observations throw doubt on the validity of the hypnotic re-living of past events, which may also be no more than an enactment of fantasied experiences, though the authors doubt whether this is likely in the case of past events of a traumatic emotional significance. *F. K. Taylor*

1131. **Psychological Correlations with Secondary Amenorrhea**
K. KELLEY, G. E. DANIELS, J. POE, R. EASSER, and R. MONROE. *Psychosomatic Medicine* [*Psychosom. Med.*] **16**, 129–147, March–April, 1954. Bibliography.

In a study carried out at Columbia University, New York, to determine whether there is any correlation between the occurrence of secondary amenorrhoea and the presence of psychopathological factors, 26 women with secondary amenorrhoea (S Group), and 20 normal women of similar age (N Group) were given a psychiatric examination. Amenorrhoea in the S group had been present for 6 months or more, and no organic cause for it could be found. All the women were interviewed at least three times. The authors' conclusions are based mainly on the findings in 12 members of the S group who were intensively studied, and these were designated the "A series".

The incidence of psychosexual immaturity, as shown by sexual inhibition, rejection of the female role, and anxiety over sexual activity, was much higher in the A Series than in the N Group, and orgastic potency much lower. Oral conflict, as shown by confession of compulsive overeating and confirmed by observations made at interview, was much more often found in the A Series; in this group also there was a high incidence of "schizoid thinking" as revealed by paranoid ideas, impairment of sense of reality, and other traits. Among the S group, temporal correlations were often encountered between the cessation of menses and the emergence, or threatened emergence, of emotional conflict. The literature on secondary amenorrhoea is extensively reviewed.
Desmond O'Neill

1132. **On the Glucose Tolerance Test, and the Effect on the Formed Elements of the Blood of Glucose and Epinephrine in Schizophrenia**
D. A. FREEDMAN, M. SABSHIN, H. E. KING, and B. O'REARDON. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **119**, 31–42, Jan., 1954 [received May, 1954]. 5 figs., 14 refs.

The authors have analysed the results of glucose tolerance tests on 10 schizophrenic patients and 10 healthy controls at Tulane University School of Medicine, New Orleans. The tests included an oral one-dose and two-dose (Exton–Rose) and an intravenous glucose tolerance test, as well as the Thorne test with injection

of 25 mg. of adrenaline. Lymphocyte and eosinophil counts were determined on each specimen of blood withdrawn. The results showed that in response to the Exton–Rose test there was a slower rise and a lower peak in the glucose tolerance curve of the schizophrenic patients as a whole compared with that of the controls. There was also a lower peak in the curve of the schizophrenic patients in response to the one-dose oral test. No appreciable difference was observed between schizophrenic patients and controls in the curve of response to the intravenous glucose tolerance test.

The authors conclude that a delay in absorption of glucose from the intestine is an associated disorder in schizophrenia, and they discuss the possible factors involved. The changes in the eosinophil and lymphocyte counts were similar in the two groups; neither glucose nor adrenaline appeared to constitute a sufficient stress for the differentiation of schizophrenic patients from controls when the response of formed blood elements was used as an index of adrenal response.

J. B. Stanton

MENTAL DEFICIENCY

1133. **An Experiment in the Treatment of Masturbation in Oligophrenia**

G. DE M. RUDOLF. *American Journal of Mental Deficiency* [*Amer. J. ment. Defic.*] **58**, 644–649, April, 1954. 5 refs.

In view of the fact that masturbation is common among low-grade male mental defectives and of the possibility that this activity may contribute some additional mental dullness, the author has investigated the effect of stilboestrol in reducing the frequency of the practice. Only 6 patients were treated, and 4 of these were initially given a placebo in an effort to achieve a controlled experiment. Each patient was given 0·25 mg. of stilboestrol up to three times daily and the frequency of masturbation observed over periods varying from 21 to 66 weeks. The results are analysed statistically in detail, with due regard to the season of the year. During the course of treatment some increased mental activity was observed, but the frequency of masturbation was reduced in 2 patients only.

[The author does not say whether he considers that such treatment with small doses of stilboestrol is worth while.] *L. G. Kiloh*

1134. **The Etiology of Mongolism**

L. LANDE-CHAMPAIN. *Journal of Child Psychiatry* [*J. Child Psychiat.*] **3**, 53–69, April, 1954. 13 refs.

From a study of the maternal history in 150 cases of mongolism the author sets out to show that the mongoloid develops as a result of fertilization of a subnormal ovum near the lower margin of fertility. He divided the cases according to the factors responsible for temporary or permanent ovarian dysfunction into three groups: (1) " near-physiologic " exhaustion (22 cases); (2) primary ovarian dysfunction (60 cases); and (3) secondary ovarian dysfunction (68 cases). There was also a small group of 7 cases in which the ovarian dysfunction was unexplained. (A footnote to a table points out that 7 cases are included in both Groups 1 and 2, since primary and secondary dysfunction appeared to be of equal importance in these cases.)

In all the women in Group 1 there was exhaustion of an originally efficient reproductive system through overwork up to the menopause. Most of the women in Group 2 had " difficulty in becoming pregnant " or experienced long intervals of involuntary sterility; 13 of the patients in this group with transitory dysfunction were adolescents. The conditions responsible for the secondary ovarian dysfunction in Group 3 included thyroid deficiency, acute or subchronic diseases, a too-rapid succession of pregnancies, local disorders of ovaries or tubes, and psychological disturbances at the time of conception. Advanced maternal age was not a significant factor, although " function " age was important. A highly-strung, nervous personality was noted in 72 of the 150 mothers in this series.

The question whether the ovarian factors operate only if a hereditary one is present at the same time cannot as yet be decided. *G. de M. Rudolf*

1135. **The Problem of the Medical Treatment of Mental Deficiency in Children.** (Zum Problem der medikamentösen Behandlung des Schwachsinns bei Kindern)

H. KOCH. *Archiv für Psychiatrie und Nervenkrankheiten, vereinigt mit Zeitschrift für die gesamte Neurologie und Psychiatrie* [*Arch. Psychiat. Nervenkr.*] **191**, 463–477, 1954. 27 refs.

DRUG ADDICTION AND ALCOHOLISM

1136. **Barbiturate Addiction Simulating Spontaneous Hyperinsulinism**

R. A. HUNTER and H. P. GREENBERG. *Lancet* [*Lancet*] **2**, 58–62, July 10, 1954. 23 refs.

Barbiturate addiction is a growing problem and its results are more harmful than those of addiction to morphine, yet insufficient attention is paid to the incidence and effects of barbiturate intoxication. In the present paper 3 cases of drug addiction simulating spontaneous hyperinsulinism are reported from Guy's Hospital, London.

The first patient was a medical auxiliary, a single woman aged 30 years. She complained of attacks of sleepiness, hunger, and feelings of detachment. A glucose tolerance test showed a hypoglycaemic level, but this was not confirmed when the test was repeated. It was discovered that the patient was taking 20 to 30 grains (1·3 to 2 g.) of barbiturate daily. Increase in dosage gave rise to increased frequency and duration of the attacks, and she often threatened to commit suicide. She complained of insomnia and muscle pains—symptoms characteristic of the withdrawal stage of drug addiction.

The second patient was a medically qualified dentist aged 36 who suffered from attacks of sweating, trembling, hunger, ataxia, and incoherence. At times he lost con-

sciousness and became incontinent. Taking food or glucose brought relief. Laboratory investigation failed to reveal any abnormality in carbohydrate metabolism, and eventually a history of addiction to morphine and amylobarbitone sodium was obtained. The illness proved fatal after the patient had made two unsuccessful attempts to commit suicide, death being attributed to drug intoxication.

Severe attacks of disturbed behaviour and loss of consciousness were observed in the third patient, a student nurse aged 31. At first she was considered to be suffering from episodes of functional hypoglycaemia. Subsequently, however, she confessed to being addicted to amylobarbitone sodium. In this case, as also in the first case, electroencephalography showed the " fast activity " due to barbiturates. *A. Garland*

1137. **Some Observations on the Behavior Pattern of Alcoholics on Antabuse Therapy**
L. L. TUREEN. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **119**, 43–51, Jan., 1954 [received May, 1954]. 2 refs.

At the Jewish Hospital, St. Louis, the behaviour pattern was observed in 5 patients receiving disulfiram (" antabuse ") for alcoholism of 10 to 40 years' duration. The treatment was successful in 4 cases, and the enforced sobriety permitted psychotherapy. In the early stages the patients showed marked dependency needs which required strong support from the therapist; their desire for drink was gratified by large amounts of " soft " drinks. Of interest was the fact that in some instances a cold bottle in the hand was very comforting. If there was sufficient provocation the behaviour pattern characteristic of the alcoholic bouts was reproduced during the period of treatment, and was then accompanied by unbearable anxiety which led to attempts to escape by suicide or reversion to alcohol. It is suggested that the behaviour during alcoholism is an " acting out " of compulsive drives which are too painful to be allowed expression during sobriety. *J. B. Stanton*

1138. **Use of Chlorpromazine in Chronic Alcoholics**
J. F. CUMMINS and D. G. FRIEND. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 561–564, May, 1954. 5 refs.

The symptoms of post-alcoholic psychomotor agitation which usually accompany the " drying out " period preceding drug therapy for alcoholism are not only distressing but may deter patients from seeking treatment even when they want to. The present authors, impressed with the antiemetic properties of chlorpromazine in other conditions, tried this drug in the treatment of 60 patients at the Peter Bent Brigham Hospital (Harvard Medical School), Boston, who were suffering from acute or chronic alcoholism, some with delirium tremens.

Treatment was as follows. Irrespective of the amount of liquor the patient had consumed a dose of 100 mg. of chlorpromazine was given simultaneously with 500 mg. of disulfiram by mouth; within 6 hours a further 50 mg. of chlorpromazine was given, followed 24 hours later by 500 mg. of disulfiram with 50 mg. of chlorpromazine; 48 hours after the initial treatment 500 mg. of disulfiram with 25 mg. of chlorpromazine was administered; thereafter 500 mg. of disulfiram was given daily for a week, and at the end of that time the dose was adjusted to the patient's tolerance. When vomiting occurred 50 mg. of chlorpromazine was given intramuscularly. Some of the more dehydrated patients also had dextrose and water intravenously.

It was immediately apparent that chlorpromazine was not only effective in suppressing the nausea and vomiting of the disulfiram–alcohol reaction, but also inhibited the usual psychomotor agitation which accompanies withdrawal of alcohol. Within an hour the patient became calm, drowsy, and in some cases fell into a restful sleep which lasted 10 to 12 hours. Within 24 hours the patient was hungry and able to take solid food. Several patients were able to return to work within 72 hours without even experiencing the common tremulous sensations characteristic of the post-alcoholic state. Chlorpromazine was found to be much less effective in controls. No untoward reactions were noted.

[This appears to be a most effective method of controlling post-alcoholic psychomotor agitation and of setting the alcoholic patient on the road to recovery.]
R. J. Matthews

1139. **Vitamin Medication in Alcoholism**
M. F. TRULSON, R. FLEMING, and F. J. STARE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 114–119, May 8, 1954. 11 refs.

An investigation into the effect of multiple vitamin therapy in large dosage in treating alcoholism was undertaken at the Harvard School of Public Health and the Peter Bent Brigham Hospital, Boston. The 207 alcoholics (166 men and 41 women) taking part in the study had been seriously addicted to alcohol for some years, but were otherwise unselected. The results given represent an evaluation at the end of the second year of the investigation.

Detailed inquiry was first made into the nutritional history and drinking habits of the patients, who were then divided into two groups. One group was treated with a special vitamin regimen, and the other received placebo medicines disguised to resemble the vitamins, so that the differentiation could be kept secret from the assessors. The vitamins given included vitamin A (" aphalin "), ascorbic acid (" cevalin "), vitamin E (" eprolin "), and vitamin-B_{12} concentrate. [The complete list of medicaments and dosages is too complicated to be summarized here.]

Cooperation by the patients was poor as regards both attendance and the taking of the medicaments. During the two-year period 58% of them ceased to attend, and only 32 patients continued treatment for 13 months or more. Results are given for 159 patients (114 treated with vitamins and 45 given placebos), of whom about half completed 6 months or more of the course. Of the group receiving vitamins 16% remained abstinent and a further 17% showed some improvement in their drinking habits, leaving 67% unchanged or worse. The corresponding figures for those treated with placebos were

21%, 2%, and 77%. Those who persisted for 6 months showed fewer failures (38% in the vitamin group and 50% of the placebo recipients); after 13 months the results were better still, especially in those treated with vitamins (only 9 failures out of 25), but the diminishing numbers were disappointing. Some patients thought that vitamins diminished the desire to drink and also lessened the effect of alcohol.

The authors contend that the benefits, though meagre, justify further research on these lines. [In view of the usually poor prognosis with this kind of addiction the patients' views are interesting and appear to justify the authors' contention, even though the statistical results are not very convincing.] *R. J. Matthews*

1140. **Encephalographic Findings in Chronic Alcoholism.**
(L'indagine encefalografica nell' alcoolismo cronico)
F. SANTAGATI and D. FERRAZZI. *Nevrone* [*Nevrone*] **2**, 3–29, 1954. 16 figs., 24 refs.

TREATMENT

1141. **Intravenous Acetylcholine in Treatment of the Neuroses**
R. M. PHILLIPS and J. T. HUTCHINSON. *British Medical Journal* [*Brit. med. J.*] **1**, 1468–1470, June 26, 1954. 12 refs.

The intravenous injection of acetylcholine, a method first introduced by Lopez Ibor in Spain (*Proc. roy. Soc. Med.*, 1952, **45**, 511), was used by the authors in the treatment of 211 patients (125 men and 86 women) at St. Thomas's Hospital, London. The type of patient found to benefit most from this treatment is defined as an anxious patient of obsessive personality suffering from severe inner tension of fluctuating intensity, often with a single phobia. This type is also found among patients with anxiety hysteria accompanied by a single conversion symptom, or with alcoholism, mixed depression and obsessional tension, or schizophrenia. It is emphasized that patients with classic obsessional neurosis, polysymptomatic hysteria, and endogenous depression with retardation were all made worse by treatment with acetylcholine. Psychopathic cases and patients with eczema showed no improvement.

Treatment consisted in the intravenous injection of 200 mg. of crystalline acetylcholine in 2 ml. of distilled water, given at least one hour after a meal. It was found best to give 50 mg. slowly at first as a sensitivity test, and subsequent injections were then increased by 50 mg. at a time up to 200 mg. A few patients who were sensitive to 25 mg. or less were cautiously treated. The rapid injection of 50 mg. produced a reaction which could then be sustained by slower injection of the remaining 150 mg. The usual course was 30 injections given over 6 to 10 weeks. The response took two forms—a mild form with coughing, flushing, sweating and salivation, and momentary brachycardia, and a syncopal form, with convulsions and cardiac arrest; the first form was that aimed at. Over 6,000 injections have now been given, with no untoward incidents.

The best results were obtained in obsessional patients, 73 out of 104 (70%) being improved after the first treatment. The injections were also successfully given in conjunction with electric convulsion therapy for the reduction of tension. The treatment was found suitable for out-patients, since there are few after-effects and patients could leave hospital within 5 to 20 minutes after treatment. *E. M. Watkins*

1142. **Evaluation of Lithium in Treatment of Psychotic Excitement**
B. GLESINGER. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 277–283, Feb. 20, 1954. 1 fig., 49 refs.

The author reports, from Claremont (Western Australia) Mental Hospital, the effect of the administration of lithium citrate on psychotic excitement in 104 mental patients. Almost every psychotic syndrome, including various residual organic states, was represented among the cases. The salt, which is readily soluble, was given orally in doses of 20 grains (1·3 g.) 3 times a day for 7 to 12 days, then 10 grains (0·65 g.) thrice daily for about one month, and finally stabilization was obtained on a daily dosage ranging from 10 to 30 grains (0·65 to 2 g.). In 45% of the patients the response was regarded as " extremely good " (in the sense of diminished excitement and increased contact and cooperation), and in 28% as " good "; the drug, in the dosage used, takes some weeks to develop its sedative effect.

Toxic effects, which occurred in 10% of the cases and are discussed at some length, were mostly seen early in the series, and the author believes that better selection of cases in the light of his experience will diminish these risks. They included gastrointestinal symptoms and symptoms involving the central nervous system; one patient with encephalitis died. Transitory albuminuria also appeared, but evaluation of this sign showed its relatively innocuous nature. It is recommended that abnormally quiet, inactive, depressed patients and those with intercurrent disease, particularly nephritis, should not be treated with the drug. Development of lithium poisoning may be prevented by ensuring a high intake of sodium chloride. When toxic signs appear, the drug should be stopped, saline infusions given, and excretion promoted; when the central nervous system is involved, the intravenous use of " cylotropin ", a hexamine compound, is advocated, and the administration of sodium thiosulphate and BAL may also be of value. The author concludes that lithium therapy, previously suggested by Cade (*Med. J. Aust.*, 1949, **2**, 349), represents a step forward in the treatment of psychotic excitement in mental patients. *A. Tait*

1143. **Chlorpromazine in the Treatment of Neuropsychiatric Disorders**
N. W. WINKELMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 18–21, May 1, 1954. 10 refs.

In an investigation at Philadelphia the author attempted to assess the value of chlorpromazine (" largactil "; 10-(γ-diethylaminopropyl)-2-chlorophenothiazine hydrochloride) in the treatment of 142 patients with various

neuropsychiatric disorders, some of whom were seen in private practice, some in a hospital out-patient department, and the rest in hospital wards. This number was made up as follows: psychoneurosis, 65 patients; psychophysiological disorders, 5; schizophrenia, 15; senility with agitation, 27; manic psychosis with agitation, 10; neurological disorders (epilepsy and paralysis agitans), 12; and 8 other patients serving as an experimental group in a study of optimum dosage. The clinical characteristics of these cases are tabulated.

Treatment of patients not in hospital and of the 27 agitated senile patients was started with an oral dose of 75 mg. (25 mg. with each meal), and this was gradually increased after the first week until clinical improvement or excessive drowsiness occurred. Patients received the drug for 8 to 32 weeks, and were satisfactorily maintained on doses of 30 to 150 mg. per day. The extent of drowsiness varied greatly. Psychotics treated in hospital were given 25 mg. intramuscularly 4 times daily for the first 2 or 3 days and 50 mg. 4 times daily thereafter. Clinical response was judged according to the patient's own appraisal, comments from his or her friends and family, and psychiatric evaluation. Results of the assessment, graded into 5 degrees of improvement, are presented in a table.

Of 67 patients with severe anxiety reactions, 56 showed moderate to complete relief of symptoms; 5 of 6 patients with phobic reactions reported at least moderate relief, in one case the relief being complete; and 6 of 8 patients with obsessive thinking experienced moderate to complete relief. The author suggests that no obsessive patient ought to be subjected to frontal lobotomy until chlorpromazine has been tried first.

The condition of half of the group of agitated senile patients given oral therapy became aggravated after 3 to 7 days of treatment, followed shortly afterwards by a marked improvement. Altogether 21 of the 27 patients in this group became greatly improved and remained so for 2 months. In this connexion it is noted that chlorpromazine appears to calm patients without depressing their mental processes as do barbiturates. In 8 cases of psychosis with moderate to marked agitation in which oral doses of 100 mg. of chlorpromazine 4 times daily had failed, control was achieved with 50 to 75 mg. intramuscularly 3 or 4 times daily. In several patients paranoid delusional features were reversed. Of 6 patients with epilepsy, 4 failed to benefit from the treatment; in the other 2, good results were obtained.

Drowsiness was reported by almost all patients at the start of treatment, but this usually wore off by the end of the first week; it could be counteracted by D-amphetamine sulphate, 5 mg., or caffeine citrate, 180 mg., given with the morning and noon doses of chlorpromazine. Dryness of the mouth, bad or bitter taste, and increased frequency and intensity of dreaming were reported. Two patients had urticarial dermatitis, and 3 developed jaundice after 2 to 5 weeks' treatment. There was some suggestion that chlorpromazine may precipitate jaundice in patients with impaired hepatic function. A fall in blood pressure was observed in 7 of 8 patients after intramuscular injection of 50 mg. of the drug. There appeared to be no danger of shock, but the author recommends that patients should remain recumbent after receiving the drug parenterally. Local reactions were minimal and there were no significant changes in blood count.

In discussing the possible mode of action of chlorpromazine the author observes that when given parenterally and in sufficient dosage to psychotic or severely obsessive patients it produced an effect similar to that of frontal lobotomy. Two-thirds of the patients who experienced drowsiness acquired tolerance to this side-effect, whereas only 2 developed partial tolerance to the beneficial action of the drug. A regimen likely to reduce the incidence of drowsiness is suggested.

[No measures of significance are given, no control groups were used, and during the period of the study several complicating and uncontrolled factors appear to have been introduced.] *John C. Kenna*

1144. **The Long Term Evaluation of Prefrontal Lobotomy in Chronic Psychotics**

R. F. MEDINA, J. S. PEARSON, and H. F. BUCHSTEIN. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **119**, 23–30, Jan., 1954 [received May, 1954]. 9 refs.

In this paper from the Wilmar State Hospital, Minnesota, a controlled investigation is reported of the effect of prefrontal lobotomy on 46 patients suffering from chronic psychoses, the operation having been performed 8 to 9 years previously. It was found that 6 of the patients developed convulsions after an average of 3·3 years from the time of operation, 2 of them having the first attack between 5 and 6 years after operation. In terms of improvement, 20 of the patients derived considerable benefit from prefrontal lobotomy, 5 of them reaching the peak of adjustment within one year; 5 years after operation 12 had achieved the maximum adjustment, the remainder continuing to improve up to 8 years afterwards. In some cases a regression was subsequently observed, particularly among patients with schizophrenia, but patients with affective psychoses tended to go on improving. Although the number of patients who recovered was higher in the affective group than in the group with schizophrenia, consideration of the average degree of improvement indicated that the operation was at least as valuable in the latter group. There was a positive correlation between degree of improvement and age at the time of operation, and a negative correlation between degree of improvement and duration of stay in hospital before operation. Convulsions had no influence on the degree of improvement. The patients operated on showed significant decrease in ability on the Porteus Maze and the Wechsler Picture Arrangement tests when compared with a matched control group of psychotic patients. *J. B. Stanton*

1145. **Macroscopical Investigations of Twenty-nine Brains Subjected to Frontal Leukotomy with Some Observations on Clinico-pathological Correlations.** [In English]

N. EIE. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. neurol. scand.*] Suppl. 90, 1–40, 1954. 11 figs., 15 refs.

Dermatology

1146. **Cholinesterase Activity of Human Skin**
I. A. MAGNUS and R. H. S. THOMPSON. *British Journal of Dermatology* [*Brit. J. Derm.*] **66**, 163–173, May, 1954. 36 refs.

It has been suggested that a derangement of acetylcholine metabolism in the skin may underlie the changes occurring in certain dermatoses. In view of the controversial findings recorded in the literature regarding the presence of true and of " non-specific " or pseudocholinesterase in the human skin, the authors, working at Guy's Hospital, London, have carried out a series of experiments to clarify the position. Acetyl-β-methylcholine and butyrylcholine were used as the substrates for true and for pseudocholinesterase respectively, and 54 samples of normal skin from 15 different sites on 31 male and 23 female patients below 70 years of age were examined, 36 being obtained by biopsy under local analgesia and 18 post mortem; the method of obtaining and of preparing the samples is briefly indicated. The esterase activity was estimated by measuring the amount of carbon dioxide liberated from the medium.

The values (which are tabulated) obtained from the skin of the living subjects are contrasted with those obtained from post-mortem specimens; the biopsy material showed a marked preponderance of pseudocholinesterase activity, the values in females being significantly higher than those in the male subjects. The levels of true cholinesterase were about equal in men and women. In the post-mortem material pseudocholinesterase activity was surprisingly low in view of the fact that the activity of this enzyme in other tissues stored for one to 3 days does not decrease to a similar extent. It is suggested that possibly bacterial contamination and the low nutritional state of the patients at the time of death were responsible for the low value. Brief mention is also made of some experiments in which the pseudocholinesterase was characterized more exactly by differential hydrolysis of tributyrin and butyrylcholine; the degree of inhibition of esterase activity by eserine and by di*iso*propylfluorophosphonate was also assessed. Almost all pseudocholinesterase activity was found to be situated in the dermis, and very little in the epidermis. In 2 cases of cholinogenic urticaria the pseudoesterase levels were decreased, although they were normal in other conditions with wealing, such for example, as dermatographia.

The clinical implications of these findings and the possible reasons for the higher pseudocholinesterase level in women are discussed. Although the presence of acetylcholine in the skin has never been definitely demonstrated, the presence of cholinesterase activity is strong evidence in favour of the presence of cholinergic mechanisms. These may be concerned with the perception of pain or cold, or with vascular responses such as the flare of the " triple response " in the skin. Cholinogenic itching, it is suggested, may be due to excessive accumulation of acetylcholine in the skin due to a deficiency of cholinesterase.

Ferdinand Hillman

1147. **Eczema and Calcium Metabolism.** (Ekzem und Kalziumstoffwechsel)
A. ST. v. MALLINCKRODT-HAUPT. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **129**, 289–295, 1954. 1 fig., 41 refs.

In this paper from the Dermatological Clinic, Brühl, Germany, the author, after briefly reviewing some of the literature on calcium metabolism in relation to skin diseases, discusses a number [unspecified] of his own cases in which there was some disturbance of calcium metabolism in association with eczema. In routine estimations carried out in all cases of eczema and urticaria seen at the clinic in recent years, low serum calcium values were found in only 7% of cases of eczema, but all of these have proved resistant to routine treatment methods.

The clinical findings in these cases were not specific, but in the majority the eczema was generalized and symmetrical. The cases were divided into three groups according to the response to treatment with calcium, and illustrative case histories are given in detail. In the first group, thought to be due to deficient absorption (for example, in cases of achlorhydria), the injection of calcium alone proved rapidly effective. In the second group latent tetany was present, probably owing to a defect in utilization of calcium, and only when " A.T.10 " (dihydrotachysterol) was given in addition to oral or parenteral calcium was there any change in the skin condition, but then improvement was quick to occur. Patients in the third group were all cases of generalized, weeping, severe dermatitis associated with hypoproteinaemia, and in these the disturbance of calcium metabolism was considered to be due to a failure in transportation of the ion.

The author concludes that further investigation of the possible connexion between the skin condition and calcium metabolism in obstinate cases of eczema may lead to a useful method of treatment being discovered.

Benjamin Schwartz

1148. **Neuropathological Findings in Pemphigus Vulgaris.** (Некоторые данные по патоморфологии нервной системы при пузырчатке)
N. E. YARŸGIN and G. F. ROMANENKO. *Архив Патологии* [*Arkh. Patol.*] **16**, 52–57, Jan.–March, 1954. 7 figs., 9 refs.

In this paper the histological changes found in the peripheral nerve endings, sympathetic ganglia, ganglion nodosum, spinal cord, brain stem, hypothalamus, and cerebral cortex in 2 cases of pemphigus vulgaris are

described. The changes in the peripheral parts of the nervous system were considered to be chiefly irritative in nature. The vegetative nerve centres in the spinal cord were more involved than those of the somatic nerves. The nerve cells in the hypothalamus, the cranial nerve nuclei, and the lateral horns of the spinal cord were more affected than the peripheral ganglia, and there were therefore lesions in the preganglionic conduction fibres. Among the histological changes were beading and swelling of the nerve endings, chromatolysis and swelling of nerve cells, and occasional shrinking of the cells, with hyperchromatosis. Changes were also present in the cerebral cortex, but these were less marked than those in the hypothalamus, medulla oblongata, and spinal cord.

L. Crome

1149. **Pemphigus and the Pemphigoids.** (Pemphigus et pemphigoïdes)
A. TOURAINE. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph.* (*Paris*)] **81**, 121–146, March–April, 1954. Bibliography.

1150. **Light Sensitive Eruptions Treated with Atabrine and Chloroquine**
J. M. KNOX, J. H. LAMB, B. SHELMIRE, and R. J. MORGAN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **22**, 11–16, Jan., 1954. 12 refs.

The authors report 18 cases of light-sensitive eruption treated with mepacrine or chloroquine. The dose of mepacrine was usually 0·1 or 0·25 g. and that of chloroquine 0·25 g., twice or thrice daily, the period of treatment extending from 3 to 6 months or more. Improvement was noted in all cases. *Kate Maunsell*

1151. **Chondrodermatitis Helicis. Chondrodermatitis Nodularis Chronica Helicis**
R. SHUMAN and E. B. HELWIG. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **24**, 126–144, Feb., 1954. 11 figs., 23 refs.

The authors have studied a series of 100 histological sections taken from cases of chondrodermatitis nodularis chronica helicis recorded in the files of the Armed Forces Institute of Pathology, Washington, D.C. They also obtained clinical details from the records and from the patients or their physicians. All the patients were men, most of whom (85) came under medical observation for the condition between the ages of 20 and 59 years. The right ear was affected in 60, the left in 33, and both ears in 7. The lesions were present on the helix in 85 cases, and 90% of them were single. Pain on pressure was the characteristic symptom. A number of the patients associated the condition with sleeping on the affected ear, while others blamed tight-fitting headgear, sunburn, frostbite, or other injury.

The main histological features observed included nodular hyperplasia of the epidermis, fibrinoid alteration of the dermal collagen, proliferation of a richly vascular granulation tissue associated with an inflammatory exudate, and perichondritis with or without degenerative changes in the auricular cartilage. The aetiology is discussed.

In none of the 100 cases did the condition clear spontaneously. Surgical excision of the nodule, including the affected cartilage, proved the most satisfactory treatment. *S. T. Anning*

1152. **Treatment of Keloids with Hyaluronidase**
T. CORNBLEET. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **154**, 1161–1163, April 3, 1954. 2 figs., 4 refs.

Twenty-six patients with keloids were treated with local injections of hyaluronidase and radiotherapy; in 22 this form of treatment was coupled with surgical removal. None of the keloids recurred. Histological study furnished suggestive evidence that the enzyme interferes with the basic pattern of the keloid.—[Author's summary.]

1153. **The Development of Malignant Melanoma in Both Recipient and Donor Sites of an Autogenous Skin Graft**
H. A. S. VAN DEN BRENK. *Australian and New Zealand Journal of Surgery* [*Aust. N.Z. J. Surg.*] **23**, 313–316, May, 1954. 3 figs., 14 refs.

1154. **Localized Chromidrosis. A Survey**
W. B. SHELLEY and H. J. HURLEY. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **69**, 449–471, April, 1954. 6 figs., 42 refs.

Although chromidrosis was first described 250 years ago little is still known about it. The authors, from the University of Pennsylvania, describe a case which was first referred to them in 1949. A woman aged 29 years had suffered from "black sweat" on her cheeks since she was 19. The coloured sweat appeared after emotional and thermal stimulation and after an injection at room temperature of 0·1 ml. of 1 in 1,000 solution of adrenaline. A local injection of atropine solution failed to prevent this response to adrenaline. Histological examination of a biopsy specimen from the cheek showed that apocrine glands containing yellow-brown granules were present. The reactions to staining tests for melanin and for iron were negative, but that for lipofuscin was positive. It was concluded that the patient had chromidrosis and that the coloured sweat came from aberrant apocrine sweat glands.

Since the axilla contains the largest number of apocrine glands a local injection of adrenaline was given into the axillae of 100 male subjects. In 11 of these the pure apocrine sweat was coloured yellow, blue, green, or black. A further injection within 24 hours was without effect, but after a rest period of a week, or in some cases several weeks, coloured sweat was again observed in response to adrenaline.

The authors conclude that the colour of apocrine sweat in chromidrosis is caused by varying amounts of lipofuscin in different stages of oxidation. The higher the degree of oxidation the darker the colour. Apocrine chromidrosis is believed to be common, but rarely manifests itself clinically because apocrine sweat is produced in small quantities and is diluted with eccrine sweat.

[This is an important contribution to knowlege of this curious condition.] *S. T. Anning*

Paediatrics

NEONATAL DISORDERS

1155. **The Treatment of Neonatal Narcosis with N-Allylnormorphine: a Preliminary Report**
D. SOLOMON, A. MICHAEL, and I. A. SIEGEL. *Sina Hospital Journal* [*Sinai Hosp. J.*] **3**, 29–37, May, 1954. 16 refs.

Administration of a narcotic drug to the mother before delivery often adds to her comfort but may be harmful to the foetus. In this preliminary report the authors describe the effect on the foetus of a morphine antagonist, N-allylnormorphine (" nalline "), given to the mother before delivery. A narcotic preparation, usually 100 mg. of pethidine, was administered to 123 patients admitted to the obstetrical department of the Sinai Hospital, Baltimore, between 30 minutes and 3 hours before delivery. Of these, 65 received 10 mg. of nalline intravenously 10 to 20 minutes before delivery, while 58 served as a control group. About a third of these patients were also given nitrous oxide anaesthesia and the remainder received regional analgesia. Some of the infants were premature and these were excluded from the final analysis, which was based upon 28 patients (16 controls) who received general anaesthesia and 75 (37 controls) who received regional analgesia.

The condition of the newborn infants was evaluated according to the method of Apgar, which is based upon the infant's colour, heart rate, respiratory effort, muscle tone, and response to nasal stimulation. There was a reduction in neonatal narcotic depression in the infants of the patients given nalline, whether the latter received inhalation anaesthesia or regional analgesia. In addition, 14 infants suffering from narcotic depression were given nalline at birth directly into the umbilical vein, and all responded within 2 minutes.

The authors point out that this drug should not be regarded as a panacea for neonatal narcotic depression but should be given only as a specific antidote for opiate narcosis. *R. M. Todd*

1156. **Some Physical Factors in Resuscitation of the Newborn and a Controlled Resuscitator**
J. MANN. *British Journal of Physical Medicine* [*Brit. J. phys. Med.*] **17**, 126–132, June, 1954. 4 figs., 6 refs.

The author describes the apparatus and method used at Toronto during the past 3 years for the resuscitation of the newborn infant. The apparatus was designed to provide oxygen for intratracheal insufflation by a two-port, ball-valve single chamber with which is combined a hand suction pump to clear the airway. Metal catheters, " designed to prevent trauma ", are used for the intratracheal insufflation. The metal construction of the catheter is claimed to provide rigidity which facilitates control and, by allowing a thin wall, gives maximum lumen. Oxygen flowing at 4 litres a minute is delivered through the ball valve at a positive pressure of 12 mm. Hg and a negative pressure of 8 mm., alternating at a rate of 10 to 15 per minute. The apparatus is reported to be wholly reliable and has required no modification since its introduction. *David Morris*

1157. **Augmented Respiration. An Emergency Positive-pressure Patient-cycled Respirator**
I. DONALD. *Lancet* [*Lancet*] **1**, 895–899, May 1, 1954. 3 figs., 3 refs.

The management of respiratory difficulties in the newborn infant by augmenting spontaneous respiratory effort is described. An ingenious apparatus [for details the original paper should be consulted] provides a positive pressure synchronously with contraction of the diaphragm in inspiration, a photo-electric mechanism being used. A mixture of equal parts of oxygen and nitrogen is admitted into the apparatus from a cylinder at a pressure of 1·8 lb. per sq. inch (0·126 kg. per sq. cm.), and delivered at a pressure of about 15 cm. of water to the infant.

This method of augmenting respiration was used in 21 cases at Hammersmith Hospital, London; in 3 cases the period of gestation was less than 28 weeks, and the infant was not, therefore, viable. Of the remainder 9 survived. Necropsy examination of the 9 viable infants who died revealed intraventricular haemorrhage, atelectasis with hyaline membrane, or intrapulmonary haemorrhage. The apparatus was also successfully used on a woman of 62 whose respiration failed after operation. *David Morris*

1158. **Gastric Suction in Infants Delivered by Caesarean Section**
L. C. FREEMAN and R. B. SCOTT. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **87**, 570–574, May, 1954. 7 refs.

At Freedmen's Hospital (Howard University College of Medicine), Washington, D.C., the authors studied the amount of gastric fluid and the effect of its removal by gastric suction in preventing pulmonary aspiration and asphyxia in three groups of newborn infants: (I) 100 infants delivered by Caesarean section who were treated by gastric suction immediately after birth and again after 4 hours and 8 hours; (II) 92 infants delivered by Caesarean section who were not treated by gastric suction; and (III) 52 infants delivered normally who were treated as in Group I. Gastric suction was carried out with a No. 10 F soft rubber catheter and a 20-ml. syringe.

It was found that the average volume of the gastric contents at birth in infants delivered by Caesarean section was 6·2 ml., compared with 3·6 ml. in the case of infants delivered normally. Whereas 24 infants in Group I and 15 of those in Group II had respiratory difficulty at birth, 17 others in the latter group developed difficulty within

the first 48 hours of life, but there were no further cases in the former group. The volume of the gastric contents at birth in Groups I and II did not appear to be influenced by preoperative medication or anaesthesia, nor by the nature of the condition which made Caesarean section necessary (apart from maternal diabetes, in which case it was considerably increased). There was a high correlation between the birth weight and the volume of the gastric contents.

The authors consider that these results suggest that the routine performance of gastric suction on all infants delivered by Caesarean section would do much to prevent respiratory complications, especially in larger infants. *Elaine M. Osborne*

1159. **The Physiologic Closure of the Ductus Arteriosus in Newborn Infants: a Preliminary Report**
F. L. ELDRIDGE, H. N. HULTGREN, and M. E. WIGMORE. *Science* [*Science*] **119**, 731–732, May 21, 1954. 13 refs.

In order to determine the exact time of closure of the ductus arteriosus the authors, working at Stanford University, San Francisco, made single estimations of the oxygen saturation of arterialized capillary blood from the right hand and one foot of 11 normal human infants at intervals after birth ranging from 1 to 108 hours; on a twelfth infant 3 estimations were made, at 2, 46, and 118 hours respectively after birth. The oxygen content and capacity of each sample of blood were measured by the Roughton–Scholander microtechnique, differences in oxygen saturation of 2·5% or less not being regarded as significant.

In all of 5 blood samples taken from the foot 1 to 3 hours after birth the oxygen saturation was significantly lower than that in blood taken from the hand; this state of affairs was also present in 3 of the 5 cases in which blood samples were taken between 3 and 72 hours after birth, but no significant difference in oxygen saturation between blood from the hand and foot was found in any of the samples taken subsequently.

The authors conclude that the ductus arteriosus remains patent and is the site of a right-to-left shunt (as in the foetus) in most infants during the first 3 hours of life, and in a significant number up to the age of 3 days, whereas in most infants more than 3 days old either the ductus has closed or the direction of flow in it has become reversed. Further and more accurate studies are in progress. *D. Emslie-Smith*

1160. **Influence of the Pre-natal Environment on Post-natal Growth**
R. H. CAWLEY, T. MCKEOWN, and R. G. RECORD. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **8**, 66–69, April, 1954. 4 figs., 9 refs.

The authors contrast the prenatal and postnatal effects of certain environmental factors on the development of children, the three factors here considered being: (*a*) duration of gestation, (*b*) birth rank, and (*c*) maternal age. The data used related to 641 out of a total of 1,327 children born in Smethwick County Borough (Birmingham) in the 12 months ending March 31, 1950 [possibly a select sample]. Total and partial correlations were calculated between indices of the environmental factors and the development (as indicated by weight and length) at birth (prenatal influence) and at 3, 6, 9, 12, and 24 months of age (postnatal influence).

At birth the correlation between duration of gestation and both infant weight and length was of the order of +0·4, declining steadily with age to +0·1 at 24 months. Thus, while duration of gestation is associated positively with prenatal development (as measured by birth weight and length), it has little influence on postnatal development. The correlation between birth rank and prenatal development was positive at birth (about 0·2), but became negative at 6 months, and at 24 months was of the order of −0·2. This the authors explain in terms of progressively unfavourable conditions for every additional child in poorer families and of the higher proportion of first-born children amongst the well-to-do. [It would have been interesting to see the results of these correlations if social class had been held constant.] Maternal age exerts no influence on prenatal development (correlations negligible at birth), but does so slightly after birth—again possibly because of a relation between maternal age at childbirth generally and social class.
E. Lewis-Faning

CLINICAL PAEDIATRICS

1161. **Infantile Eczema Treated with Oral Cortisone. A Clinical Report**
B. SOLOMONS. *British Medical Journal* [*Brit. med. J.*] **1**, 1190–1192, May 22, 1954. 5 refs.

Experience of the administration of cortisone to infants and young children suffering from severe atopic eczema is reported. The drug was given by mouth in a dosage of 75 mg. daily to 12 patients and 87·5 mg. daily to 3 others for periods of one to 3 months. A lasting and satisfactory response appeared to be obtained in 3 children; in 6 there was some improvement and in 6 the treatment was without effect. Some improvement in the general condition and well-being was observed in the majority of the children. Toxic effects were not important. *Winston Turner*

1162. **Cardioesophageal Relaxation in Infants**
K. GLASER, E. FREUNDLICH, and A. SCHWARTZ. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **87**, 586–593, May, 1954. 3 figs., 18 refs.

The authors report 3 cases of persistent vomiting in infants seen at the Hadassah University Hospital, Jerusalem, which they ascribe to a disturbance of the normal closing mechanism of the cardia. In all cases the vomiting was recurrent and not projectile, and in one case haematemesis and melaena occurred. Two of the children, aged 1 month and 2½ months respectively, were malnourished, but the other, aged 6½ months, had gained weight satisfactorily despite recurrent vomiting.

In each case a definite diagnosis could be made on radiological examination. When the child was given a thick barium paste to swallow in the erect position, the barium was seen to pour into the stomach without any

definite peristalsis; the child was then placed supine, when the barium flowed back into a dilated oesophagus, disclosing a patulous cardio-oesophageal junction. Not one of a control series of normal infants similarly examined showed such a reflux. The condition can be differentiated from sliding hiatus hernia, which causes similar symptoms, by repeated *x*-ray examination, when it is found that in cases of cardio-oesophageal relaxation the oesophago-gastric junction is always below the level of the diaphragm. The authors suggest that whatever the original cause of the regurgitation, be it disturbed autonomic balance or increased gastric pressure, the reflux of acid gastric juice produces an oesophagitis with ulceration which may further disturb the closing mechanism of the cardia.

In all cases the symptoms were relieved and the condition eventually cured by sitting the child in an upright position after meals and, at first, throughout the day. It is suggested that many cases of persistent vomiting in infants may be due to a slight degree of cardio-oesophageal relaxation. *Elaine M. Osborne*

1163. **Resistance of the Breast-fed Infant to Gastro-enteritis**

C. A. C. Ross and E. A. Dawes. *Lancet* [*Lancet*] **1**, 994–998, May 15, 1954. 3 figs., 20 refs.

In an investigation carried out at the University of Glasgow into the relative resistance of the breast-fed infant to gastroenteritis the influence of certain factors in the intestinal environment on the growth of three type strains of *Bacterium coli* (O 111, O 55, and O 26) and an untypable strain from a healthy artificially fed infant was studied. In a simple synthetic medium, nutrient broth, and nutrient glucose broth the growth of each of the four strains was negligible when the initial *p*H was below 5, the optimum *p*H being above 7. It was therefore concluded that the low *p*H of the breast-fed baby's stool would inhibit the growth of these organisms. Even a single supplementary feed of cow's milk caused an immediate rise in the *p*H of the faeces, which would favour the growth of pathogenic strains. It was also found that formic acid, which is toxic to *Bact. coli* at a low *p*H, was present in much higher concentration in the faeces of breast-fed than of artificially fed infants.

An attempt was made to lower the *p*H of the stools of artificially fed babies by giving lactose, which is present in human milk in higher concentration than in cow's milk, but the effect was only partial and temporary. The authors therefore conclude that human milk contains some other factor necessary for the maintenance of an acid *p*H and a lactobacillary flora in the faeces.

R. S. Illingworth

1164. **Obstructive Jaundice in Infants with Normal Biliary Tree**

R. C. Harris, D. H. Andersen, and R. L. Day. *Pediatrics* [*Pediatrics*] **13**, 293–307, April, 1954. 1 fig., 25 refs.

Although the symptoms of obstructive jaundice due to biliary atresia are similar to those of biliary obstruction due to other causes in infancy, the treatment required differs radically, a potentially dangerous operation being essential in the former condition, whereas cases of other types frequently make a spontaneous recovery. An accurate diagnosis of the cause of the biliary obstruction is therefore most important, and the present authors, contending that the systematic use of laboratory tests will greatly assist in differentiating cases of biliary atresia from those in which the biliary tree is normal, describe their findings in 50 cases of the latter type which were investigated at the Babies Hospital (Columbia University), New York. This total was made up of: (1) 3 infants with haemolytic anaemia; (2) 16 with erythroblastosis foetalis; (3) one with probable serum hepatitis; and (4) 30 with hepatitis of unknown aetiology, probably toxic.

In all 50 cases the clinical findings were similar to those in cases of bile-duct atresia—jaundice, enlarged liver and spleen (in some cases), dark urine, and pale stools. The general condition was good in all the infants except those with toxic hepatitis, who were thin and dehydrated. The laboratory tests performed, the results of which were similar in all groups, included estimation of the serum bilirubin level (usually high direct) and cholesterol ester content (low), the cephalin flocculation reaction (usually negative) and zinc sulphate turbidity test (value often raised), and determination of the urinary urobilin content (absent or increased). Evidence of Rh or ABO incompatibility with the maternal blood, of increased haematopoiesis, and of the presence of abnormal agglutinus was also sought for. Determinations of the serum alkaline-phosphatase level and cholesterol esterase activity and of the prothrombin time were not found to be useful.

The liver was examined histologically in 26 cases, either by biopsy or at necropsy, the findings, which were similar in all cases, including the presence of multinucleated giant liver cells, much erythropoiesis and myelopoiesis, plugging of the canaliculi, mild bile-duct proliferation, and the presence in the liver cells of much yellow pigment which did not take iron stains. Tabulation of these results makes it clear that it is only by a combination of several tests and investigations that the distinction of these cases from those due to biliary atresia can be made. If by the age of 4 months no diagnosis has been made by this means, surgical exploration, with examination of a frozen section of the liver and cholangiography carried out at operation, may be necessary.

From their results and the reported findings of other workers in different types of hepatitis the authors conclude, with Lightwood and Bodian, that the liver in this age group responds in the same way to many different types of insult. *E. M. Watkins*

1165. **Acute Bronchiolitis Treated with Detergent Aerosols**

B. Gans. *Lancet* [*Lancet*] **1**, 1011–1012, May 15, 1954. 7 refs.

Two epidemics of acute bronchiolitis chiefly affecting children under 2 occurred in south-east London during the winters of 1952–3 and 1953–4. In the first epidemic, involving 41 children, treatment consisted in administration of antibiotics and oxygen; 9 of the children died.

In the second epidemic 20 of the 27 children affected were given various detergent aerosol vapours as well as antibiotics and oxygen; none of these children died.

[It is difficult to assess the result of aerosol treatment from this paper, because epidemics of infectious diseases vary so much in severity. The difference in mortality might well have been due merely to the occurrence of a less virulent form of bronchiolitis in the second epidemic.]

R. S. Illingworth

1166. **Surgical Treatment of Acute Osteitis in Childhood**
A. E. Bremner, G. A. Neligan, and C. K. Warrick. *Lancet* [*Lancet*] **1**, 953–957, May 8, 1954. 16 refs.

The question of the urgency and extent of surgical intervention in the treatment of acute haematogenous osteitis has long been debated. The authors therefore undertook, at the Royal Victoria Infirmary, Newcastle upon Tyne, a controlled trial in which alternate patients aged 2 to 12 years were treated either by open operation and drilling of the bone or by repeated subperiosteal aspiration of pus, both groups receiving penicillin. Out of 96 cases treated during the 3 years 1949–51, the results in only 23 cases are considered here, the small number being due to the strict criteria which were applied; these were: (1) that the infection was severe, (2) that no previous antibiotic treatment had been given, (3) that treatment was begun between 48 hours and 7 days after the first symptoms had appeared, and (4) that the focus of infection lay in the femur or tibia.

The authors conclude that aspiration achieves comparably good results and, as it is the more conservative method, deserves preference since it makes the giving of a general anaesthetic to these severely ill children unnecessary. But aspiration must be performed early and repeatedly and daily expert assessment of the patient's condition in the early stages is essential.

[The details ought to be studied in this admirable account of a well-conducted trial.] *L. Michaelis*

1167. **Disseminated Sclerosis in Childhood.** (La sclérose en plaques chez l'enfant)
M. Bonduelle, P. Bouygues, and C. Sallou. *Presse médicale* [*Presse méd.*] **62**, 563–564, April 14, 1954. 8 refs.

The authors describe a typical case of disseminated sclerosis in a boy which began in childhood and which they have followed up for over 12 years. The illness started at the age of 7 as a left optic neuritis. Examination showed impairment of vision, slightly enlarged retinal veins, and blurring of the edges of the optic disk on the left side. After 3 months there was apparently full recovery and the patient remained free of symptoms for 5 years. At the age of 12, however, a paresis of the right lower limb developed, which lasted for 3 weeks. A third attack occurred at the age of 16, 9 years after the onset of the illness, in which there was pyramidal paresis of the left lower limb and paralysis of the right 6th cranial nerve. The patient recovered after 5 months, only to relapse again a month later, when he manifested disturbance of gait and impairment of sensation in the lower limbs. Since then there has been no full recovery and the disease has followed a fluctuating course, with progressive involvement of the optic, cerebellar, and pyramidal tracts.

At present the patient, now aged 19, shows a bilateral pyramidal syndrome, with spasticity, increased tendon reflexes, clonus, bilateral Babinski responses, and absent abdominal reflexes. There is also a cerebellar syndrome, with intention tremor, scanning speech, nystagmus, and ataxia; this last, added to the spasticity, renders walking almost impossible. Bilateral optic neuritis is present, more marked on the right side, vision is impaired, and there is pallor of both disks. Clinical and laboratory findings have excluded congenital syphilis, Friedreich's ataxia, and acute ataxia.

The authors claim that such a typical picture of disseminated sclerosis is rarely found in childhood. They quote several statistical studies and point out the difficulties in assessing the figures given. The relationship between disseminated sclerosis and the other demyelinating diseases is discussed. The authors suggest that the diagnosis of disseminated sclerosis in childhood should be restricted to typical cases which run a chronic course, and deplore the inclusion of cases presenting an acute and atypical picture which only brings further confusion to the problem of the demyelinating diseases in childhood.

Richard de Alarcón

1168. **Maternal Rubella and Congenital Defects**
C. M. Brown and B. J. Nathan. *Lancet* [*Lancet*] **1**, 975–976, May 8, 1954. 3 refs.

Rubella has been a notifiable disease in the City of Manchester since 1916. In 1946 a survey was carried out by the then city pathologist based on the results of necropsy of 35 infants who had died in hospital and who had some congenital malformation; in none of these cases, however, was there a history of rubella in the mother during pregnancy. A retrospective analysis was made by the present authors during 1952 of the records of rubella notifications for the period 1936–51 in respect of females aged 15 or more, of the notifications of birth in the corresponding years, and of any records of congenital malformations in the children. Again the results were negative.

It was therefore decided to ascertain first the incidence of rubella during pregnancy and then to seek for congenital abnormalities. For the year 1952, 28 women who were pregnant during the time of rubella infection were traced. There were 5 cases (17·9%) of gross congenital abnormality, such as cardiac malformations, cataract, and in one case anencephalus, in the infants of these mothers. In 13 of the 28 cases the rubella occurred before the 13th week of pregnancy and the 13 infants of these pregnancies included 4 (30·8%) of those with congenital abnormalities. For comparison, the number of cases of congenital abnormality among the 12,367 live-born babies in Manchester in the same year was 245 (2%). Pointing out that this report is provisional, the authors agree that the smallness of these figures limits their value, but believe that the difference between 17·9% and 2% is strongly suggestive of an effect of rubella in the causation of congenital abnormalities.

Jas. M. Smellie

Medical Genetics

1169. **A Hereditary Factor in Chondrodystrophia Calcificans Congenita**
F. C. FRASER and J. B. SCRIVER. *New England Journal of Medicine* [*New Engl. J. Med.*] **250**, 272–277, Feb. 18, 1954. 2 figs., 35 refs.

The authors, writing from McGill University, Montreal, describe the cases of 2 infants, a brother and sister, in whom the typical features of chondrodystrophia calcificans congenita were demonstrated radiologically and, in one case, confirmed at necropsy. The patients were the first and third children of healthy, unrelated parents, and both died within 4 weeks of birth. The other child was normal.

A review of the literature of this rare disease shows that of 33 families reported, 6 contained more than one case, 6 out of 36 siblings of propositi being affected. An analysis of the familial distribution of the disease shows that the number of affected children is almost identical with that to be expected if the condition is inherited as a simple Mendelian recessive character. *Harry Harris*

1170. **Genetic Aspects of the Primary Myopathies; Progressive Spinal Atrophy of Infants (Werdnig–Hoffman), and Neural Atrophy (Charcot–Marie–Tooth).** (Aspects génétiques des myopathies primitives, de l'atrophie spinale progressive infantile (Werdnig–Hoffman) et de l'atrophie neurale (Charcot–Marie–Tooth))
E. HANHART. *Acta neurologica et psychiatrica Belgica* [*Acta neurol. psychiat. belg.*] **54**, 91–119, Feb., 1954. 6 figs., bibliography.

The author reviews the literature on the inheritance of the progressive muscular dystrophies, with special reference to his personal experience in Switzerland. He agrees with Becker that the essential clinico-genetic division in this group of disorders is between the scapular form—which is usually determined by a dominant gene—and the pelvic form, which may be determined by either a sex-linked or an autosomal recessive gene. The sex-linked form presents a uniform clinical picture, with early onset, symmetrical distribution, constant pseudo-hypertrophy of muscles, bony dystrophy, and simple dementia; these patients usually die before the age of 30. The recessive form presents a much more varied clinical picture, although it is generally uniform within the same family. It is not yet certain whether there are, as Becker suggests, instances of muscular dystrophy due to environmental causes. (The distal myopathy of late onset, affecting the small muscles of the hands and feet and the extensor muscles of the forearm and legs, which has been described by Swedish authors, is a separate entity.)

The progressive muscular atrophies form an entirely distinct group from the muscular dystrophies, being primarily lesions of the central nervous system. Infantile progressive muscular atrophy is determined by a recessive gene. It is not yet certain whether there is a separate condition—with a relatively good prognosis—of the type that has been labelled amyotonia congenita. No post-mortem evidence is yet available, but the author believes that, though very rare, the condition probably does exist. Peroneal muscular atrophy (the neural atrophy of Charcot–Marie–Tooth) had not been recognized in Switzerland in more than one member of a family until 1951, when two separate families, each with several members affected, were discovered by Hadorn and described by Stücki and Luban (*Schweiz. med. Wschr.*, 1953, **17**, 404). The present author emphasizes that the genetic findings are important in the classification of disorders of muscles. *C. O. Carter*

1171. **A Report of Seven Cases of Chondro-osteodystrophy (Morquio's Disease)**
W. F. TOWNSEND-COLES. *Archives of Diseases in Childhood* [*Arch. Dis. Childh.*] **29**, 7–11, Feb., 1954. 17 figs., 5 refs.

The 7 cases of chondro-osteodystrophy (Morquio's disease) described in this paper from the Civil Hospital, Khartoum, are believed to be the first reported cases occurring in Sudanese families. The parents of the first family were first cousins once removed, and the second and sixth out of 7 children were affected. The parents of the second family were first cousins, and the fourth and sixth of a family of 6 children were affected. The parents of the third family were again first cousins, and the second, third, and fourth children out of a family of 5 were affected; the father had 7 normal children by another wife, to whom he was not related. The history of these patients who were of both sexes and the offspring of nearly related parents supports the view that Morquio's disease is usually due to a recessive gene, although Jacobsen (*J. Amer. med. Ass.*, 1939, **113**, 121) described a family in which the inheritance was that of a sex-linked recessive gene. *C. O. Carter*

1172. **Osteogenesis Imperfecta Congenita in Consecutive Siblings**
A. A. GOLDFARB and D. FORD. *Journal of Pediatrics* [*J. Pediat.*] **44**, 264–268, March, 1954. 1 fig., 5 refs.

1173. **Familial Koilonychia.** (Über familiäre Koilonchie)
G. WESENER. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **129**, 513–517, 1954. 7 figs., 26 refs.

1174. **Recurrent Peripheral-nerve Palsies in a Family**
D. M. DAVIES. *Lancet* [*Lancet*] **2**, 266–268, Aug. 7, 1954. 1 fig., 6 refs.

See also Gastroenterology, Abstract 1022.

Public Health

1175. **Public Health Aspects of Infective Hepatitis.** (Hygieniskepidemiologisk vurdering av infeksiøs hepatitt)

H. NATVIG and R. A. JENSEN. *Nordisk Medicin* [*Nord. Med.*] **51**, 432–439, March 25, 1954. 19 refs.

Writing from the University Institute of Hygiene, Oslo, the authors report that since 1942, when infective hepatitis became notifiable in Norway, its incidence has fallen from 5·6 per 1,000 in the towns, 10·14 in rural areas, and 8·87 for the whole country to 0·28, 0·23, and 0·24 per 1,000 respectively in 1952; a slight increase occurred in 1953. Between 1942 and 1946 the disease was more frequent in rural areas, but from 1947 onwards the incidence has been higher in urban areas. The mortality per 1,000 notified cases, however, has risen from 5·7, 3·8, and 4·1 for towns, rural areas, and the whole country respectively in 1942 to 36·8, 31·9, and 33·9 in 1950; the increase, it is suggested, may be due either to a rise in the number of cases of inoculation hepatitis or to the involvement of older age groups. Of 316 cases of hepatitis notified in the city of Oslo between 1949 and 1952, 170 were considered to be probably cases of epidemic hepatitis, 70 probably inoculation hepatitis, and the remainder possibly inoculation hepatitis. Details of the attack rates according to sex and age groups are given in 13 tables. *D. J. Bauer*

1176. **Epidemic of Infective Hepatitis in an Oxford College**

G. A. BALLANCE. *British Medical Journal* [*Brit. med. J.*] **1**, 1071–1074, May 8, 1954. 1 fig., 19 refs.

Investigations stimulated by the high incidence of infective hepatitis in the British and United States Forces during the second world war confirmed the importance of personal contact, direct or indirect, in the spread of this disease. But although food-, milk-, and water-borne outbreaks have occasionally been reported, it has rarely been possible to identify the exact route of infection in each case. The outbreak which is dealt with in this paper occurred among undergraduate members of an Oxford college, 47 of whom developed the disease between May 22 and June 10, 1950, the dates of onset of these primary cases being symmetrically distributed about a single peak (11 cases on May 28). The explosive nature of the outbreak suggested a food- or milk-borne infection, but inquiries among the kitchen staff failed to reveal any case of jaundice or " gastric 'flu " which might have been the original source of the infection. It was found, however, that the daughter of one of the college scouts, who developed jaundice on May 29, had visited her father in the college on a single occasion on April 29, when she had been given a plate of fruit salad and custard which had been left over from dinner the previous night.

Further investigation showed that all the undergraduate patients had either dined in hall on April 28 or lunched there on April 29, when custard was again served, to which some of that left over from the night before might have been added. Moreover, a guest from another college had been present at dinner on April 28 and had subsequently developed jaundice. The custard being the only food common to all cases was therefore presumed to have been the source of infection, although it was not discovered how contamination might have taken place. The absence of cases among the 6 members of High Table and the kitchen staff of 15 or so was explained by the fact that the former had ice-cream instead of custard with their fruit salad—as, presumably, did any of the latter who ate in the kitchen. The number of persons at risk is estimated to have been about 150, and about 1 in 3 appear to have succumbed to the hazard. There were 3 secondary cases.

The incubation period, which could thus be precisely determined, ranged from 23 to 42 days, which is consistent with the findings in other epidemics. The urine became bile-stained some time between the second and eleventh days of illness, but as a rule the patient was feeling better by the time the jaundice appeared. Two patients relapsed, one severely.

Apart from the victims of this outbreak, the author has records of only 6 cases of infective hepatitis among rather more than 1,000 cases of all kinds of illness among undergraduates seen during 1946–50. *J. Cauchi*

1177. **Control of Cerebrospinal Meningitis Epidemics with Sulfadimidine and Penicillin. Report on an Experiment in Mass Chemoprophylaxis in the Sudan**

A. MACCHIAVELLO, W. OMAR, M. A. EL SAYED, and K. A. RAHMAN. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **10**, 1–34, 1954. Bibliography.

Epidemics of cerebrospinal meningitis have been known to occur in the Sudan since the end of the last century, and during the latest series of outbreaks, from 1949 to 1952, 60,000 cases were notified. With the introduction of sulphonamides the fatality rate has fallen from 60 to 75% to a little over 10%, but from the economic point of view these epidemics continue to present a serious problem, increasing the disability among workers just at the time when extra labour is needed to help with the cotton crop and throwing a heavy burden on the resources of the Sudan Medical Service. For this reason experiments in mass prophylactic treatment with sulphonamides and penicillin have been carried out in four villages to determine the effectiveness of these drugs in the control of cerebrospinal meningitis. In one of the villages sulphadimidine (" sulphamezathine ") was given orally in a single dose of 4 g. to adults, 2·5 g. to children from 5 to 15 years, and 1·5 g. to those below 5 years of age, 93% of the population of about 1,900 being treated. In

another village, with a population of about 4,700, sulphadimidine was given in half the above dosage to 34% of the inhabitants. In the two remaining villages (populations 1,300 and 2,300 respectively) procaine benzylpenicillin with 2% aluminium monostearate (PAM) was injected intramuscularly in single doses of 150,000, 100,000, and 75,000 units according to age, 38% and 90% of the respective populations being treated.

Analysis of the subsequent incidence of the disease among treated and untreated persons showed that the two drugs were equally effective in protecting the former group, but that treatment of part of the population had no effect on the evolution of the epidemic in the unprotected population. The incidence of the disease among protected persons was 4·86 cases per 1,000 of the total population, compared with 17·68 cases per 1,000 among unprotected persons. While it would therefore seem to be advisable to protect as many members of an infected community as possible with one or other drug, reinfection of a treated group, even when it remains in close contact with a highly infected untreated group, does not appear to occur, possibly owing to the presence of low-grade immunity in previous carriers.

Franz Heimann

1178. **Notes on the Causes of Death before and after the Age of 50.** (Alcune considerazioni sulle cause di morte prima e dopo 50 anni di età)
G. Russo. *Rendiconti Istituto superiore di sanità* [*R.C. Ist. sup. Sanità*] **17**, 302–325, 1954. 5 figs.

The author has made a comparative study of the causes of death in Italy during the two 3-year periods 1931–3 and 1947–9. The average annual numbers of deaths in the two periods were 496,532 and 598,016 respectively, and the general death rates 14·5 and 10·7 per 1,000 of the population respectively. Comparison of the two periods showed that mortality had decreased by 41·1% among persons under 50 years of age but by only 18·1% among those over 50. In 1949 the number of those over 50 had increased by 21·6%, while persons under 50 were only 9·3% more numerous than in 1931; in that year 19·4% of the population were over 50, as compared with 21·1% in 1949. In 1947–9 those aged 50 or under, who represented 78·9% of the population, suffered rather less than 40% of the total deaths.

The author has analysed the changes in the relative incidence of causes of death for those under and over the age of 50, and as a result of this study he attributes the fall in the death rate mainly to the advances made in the field of social medicine and hygiene, including the better control of infant disease, and to the great therapeutic discoveries of recent years. The five main causes of death in each group, in order of incidence, were as follows. Age group 0–50 years: (1) infectious and parasitic diseases, (2) digestive diseases, (3) respiratory diseases, (4) diseases of infancy, and (5) violent or accidental deaths; for the age group 50 and over: (1) cardiovascular disease, (2) diseases of the nervous system and sense organs, (3) malignant neoplastic disease, (4) " senility ", and (5) respiratory diseases. The increased number of deaths from cancer and other malignant disease is a real one, and cannot be explained solely by the ageing of the population. The explanation may have to be sought in the strains and stresses and in other factors of modern life. It was also notable that diseases of the blood and of the blood-forming organs now occur more often as a cause of death after the age of 50 than was the case in the years 1931–3.

The author discusses the economic and social implications which derive from having an increased proportion of aged persons in the population, and he refers to the responsibilities of the community and the state in this respect, on both humane and economic grounds.

J. Cauchi

1179. **Oxford Child Health Survey. Stature and Skeletal Maturation in the Pre-school Child**
R. M. Acheson and D. Hewitt. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **8**, 59–65, April, 1954. 4 figs., 19 refs.

This report from the Social Medicine Unit of the University of Oxford makes a contribution towards solving the general problem of what factors other than heredity determine final adult height. Between 500 and 600 children were examined at 6-monthly intervals from 18 months to 5 years of age, height and stage of skeletal maturity, *inter alia*, being recorded. When groups homogeneous as regards stage of skeletal maturity were formed (from the data for all ages taken together) it was found that in any group of equally mature children the older (the slow maturers) were taller, whereas the younger (the fast maturers) were shorter, than the average of the group. These findings, when taken in conjunction with similar results reported by other workers in regard to *pubescent* children, " imply that there is a group of children whose rapid maturation marks them out, well before they reach school age, as small adults of the future ". But if, as has been suggested elsewhere, slow skeletal development may also be due to bad environment, then, on the foregoing conclusion, where bad environmental conditions obtain, stature would be expected to be above average. Yet it is well known that bad environmental conditions are associated not with enhanced but with retarded growth.

To examine this apparent contradiction the authors proceeded to study the association between stage of skeletal development and increase in stature among the well-to-do in comparison with the poorer sections of the children studied. Only among the boys was there any evidence that skeletal development was markedly affected by social environment; and where the worst environmental conditions could be presumed (Social Classes IV and V) the boys suffered a more than proportionate slowing down of growth.

[It is a pity that this report has been so condensed as to discourage all but the most persistent students from reading it. Even the golden rule that diagrams should be regarded as subsidiary aids to the perception of, and not as substitutes for, the statistical tables has been sacrificed on the modern altar of brevity. In the absence of the basic data no critical assessment of the validity of the statistical results is possible.] *E. Lewis-Faning*

Forensic Medicine

1180. **Attempted Suicide with Insulin**
H. BLOTNER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 387–390, April, 1954. 8 refs.

In a thorough search of the literature the author was able to find only 3 reported cases of suicide and 5 of attempted suicide by means of insulin. He summarizes the findings in these cases, and reports the case of a 46-year-old non-diabetic physician who was found unconscious in his consulting room. The finding of pinpoint pupils suggested morphine poisoning, but there was no response to analeptics, and ultimately the finding of a part-empty phial of insulin indicated the real cause of the coma. The blood sugar level was found to be 42 m g. per 100 ml., and the patient's response to the administration of glucose intravenously promptly proved the diagnosis to be correct. The patient made a good recovery although he had also taken a large dose of morphine. The author emphasizes the importance of early treatment in order to avoid irreversible damage to the central nervous system and the heart, similar to that seen in cases of anoxia, which may be caused by prolonged hypoglycaemia. The duration of hypoglycaemia varies with the dose and the type of insulin, and huge doses of sugar may be required over a surprisingly long period to counteract the hypoglycaemia caused by a large dose of protamine zinc insulin. *Gilbert Forbes*

1181. **Alcoholism and Attempted Suicide**
I. R. C. BATCHELOR. *Journal of Mental Science* [*J. ment. Sci.*] **100**, 451–461, April, 1954. 11 refs.

After a review of the literature on the relation of alcohol to attempted suicide the author analyses 200 consecutive cases (92 males and 108 females) of attempted suicide admitted to the Edinburgh Royal Infirmary between 1950 and 1952. The sample is considered representative of an urban population.

There was a family history of alcoholism in 57 of the cases, the majority of the patients coming from homes "broken" from this cause. In 43 cases (30 men and 13 women) there was a personal history of addiction or of repeated excess, 23 of these patients being in a state of alcoholism at the time of the attempted suicide. A further 16 patients (10 men and 6 women) who were not addicted to alcohol were under its influence when suicide was attempted, giving a total of 39 in whom alcohol played a part. Most of the 43 patients addicted to alcohol suffered from psychopathic or depressive states and were socially and sexually maladjusted. Poisoning was the commonest method of attempted suicide, barbiturates being taken by 20 of these 43 patients and coal gas by 7.

The author discusses the underlying psychopathology, and concludes that while the "chronic alcoholic does not typically commit suicide" alcoholism is a significant factor in about 30% of the cases. In many cases alcoholism and suicide have a similar psychopathological basis, the former being a kind of "fractional suicide" or substitute. He suggests that alcohol may facilitate a suicidal attempt by releasing inhibitions, but may also render it less effective—especially in excess. Alcoholism in the parents, causing disruption of the home, may be a contributory factor to the personality disorders which end in suicide. [It is of interest that the social standing of about half of the alcoholics at the time of attempted suicide was inferior to that of their childhood. This deterioration is surely significant in the present age.]
R. J. Matthews

See also Psychiatry, Abstract 1129.

1182. **Chromosomal Sex in Transvestites**
M. L. BARR and G. E. HOBBS. *Lancet* [*Lancet*] **1**, 1109–1110, May 29, 1954. 9 refs.

The recent discovery by the senior author and his colleagues that in many species—including man—the cell nuclei in the two sexes have a distinctive morphology has already been used as a means of differentiating between different types of hermaphroditism. This work has now been extended to the study of transvestism, or eonism, a sex deviation in which the subject has an overwhelming desire to adopt the attire and be accepted as a member of the opposite sex. The sexual urge is seldom a prominent feature, and the true transvestite should be distinguished from the more objectionable homosexual and sex-urged hermaphrodite.

It has been suggested that the male transvestite may represent an extreme type of intersexuality or sex reversal in which an embryo with the XX sex-chromosome complex, which is thought to determine the characteristic morphology of the cell nucleus in the normal female, is diverted in the male direction at a very early stage. This suggestion is based on the remarkable range of intersexuality shown by Goldschmidt to exist in the gipsy moth (*Lymantria dispar* L.), in which a series of female intersexes with XX chromosomes and with increasing degrees of intersexuality leading finally to apparently normal males, and a similar series of male intersexes with XY chromosomes, can be demonstrated, the degree of intersexuality found depending on the stage of development at which sex differentiation is disturbed. In order to test the theory that a similar disturbance of sex differentiation may occur in man, skin biopsy was performed on 5 male transvestites and the epidermal nuclei studied; in each case typical male morphology was found. It is therefore inferred that these persons bear the XY chromosome and are male pseudohermaphrodites. The authors point out, however, that the possibility that the abnormality may have a genetic basis is by no means ruled out, since the detection of gene changes lies far beyond the present "relatively crude method of studying intermitotic nuclei". *Keith Simpson*

Aviation Medicine

1183. **Animal and Human Reactions to Rapid Tumbling**
H. S. Weiss, R. Edelberg, P. V. Charland, and J. I. Rosenbaum. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **25**, 5–22, Feb., 1954. 12 figs., 20 refs.

Tumbling may occur at rates up to 240 r.p.m. during free fall or partially stabilized fall after emergency ejection from high-speed aircraft. The effects of the resultant accelerative forces have been studied in anaesthetized dogs and in man at the Wright–Patterson Air Force Base, Ohio. Simple tumbling in the absence of a linear decelerative field was studied by means of a rotating table, the observations made including the continuous recording of arterial and venous pressures. In anaesthetized dogs rotation about an axis passing through the heart produced a reduction in cardiac output at speeds above 75 r.p.m. and almost complete circulatory arrest above 150 r.p.m., recovery being accompanied by an " overshoot " of arterial pressure. Movement of the centre of rotation caudad reduced the circulatory effects slightly, but severe oedema of the head and neck became apparent.

Experiments on man revealed no notable circulatory impairment during rotation about the heart at speeds up to 125 r.p.m. By extrapolation, unconsciousness in man may be predicted to occur after 3 to 10 seconds at 160 r.p.m. with the centre of rotation at heart level, and at 180 r.p.m. with the centre of rotation at the level of the iliac crest (approximately the centre of gravity of the body). An almost linear relationship between log. time and rotational velocity required to produce conjunctival petechiae was noted. *D. I. Fryer*

1184. **Some Observations on Human Tolerance to Accelerative Stress. Phase II. Preliminary Studies on Primates Subjected to Maximum Simple Accelerative Loads**
E. L. Beckman, J. E. Ziegler, T. D. Duane, and H. N. Hunter. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **24**, 377–392, Oct., 1953. 5 figs., 11 refs.

Experiments are described in which the tolerance of chimpanzees to positive, negative, and transverse acceleration was investigated in a centrifuge at the University of Pennsylvania. It was found that the animal lost consciousness on exposure to a positive acceleration of between 8 and 9 *g*, and that when 15 *g* was applied for 60 seconds, loss of consciousness was accompanied by transient apnoea and a state of mild shock, from which recovery was rapid and complete. When a positive acceleration of 40 *g* was applied for 15 seconds, shock was more severe and there were numerous small haemorrhages in the legs, although the findings at necropsy in an animal killed one hour after such treatment were not considered such as to indicate permanent damage of any significance. After exposure to negative acceleration of 40 *g* for 15 seconds one animal developed massive swelling of the tongue, lower lip, and eyelids, respiratory rales, and epistaxis. No retinal haemorrhage was found, but the animal was severely shocked and remained comatose for 24 hours. By the end of a week, it appeared relatively normal. After a further exposure to negative acceleration of 40 *g* for 15 seconds, it was killed. At necropsy haemorrhages were found in the tissues of the head, neck, thorax, and pelvis, and there were extensive degenerative changes in cerebral neurones. Exposure of another animal to transverse (prone) acceleration of 40 *g* for 15 seconds had no untoward effect other than slight epistaxis. The view is put forward that a safety conversion factor of 2·5 or 3 would be appropriate in applying the findings in the chimpanzee to man.

J. A. Armstrong

1185. **Some Observations on Human Tolerance to Accelerative Stress. Phase IV. Human Tolerance to High Positive *g* Applied at a Rate of 5 to 10 *g* per Second**
E. L. Beckman, T. D. Duane, J. E. Ziegler, and H. N. Hunter. *Journal of Aviation Medicine* [*J. Aviat. Med.*] **25**, 50–66, Feb., 1954. 3 figs., 10 refs.

In further experiments at the University of Pennsylvania the duration of exposure to high positive acceleration necessary to produce unconsciousness was measured in 11 human volunteers, who were exposed to 6, 8, 10, 12, and 15 *g*, the rate of change of acceleration ranging from 3·5 to 9·6 *g* per second. The duration of exposure required to produce unconsciousness was less at the higher levels of acceleration than at the lower levels; but it was noted that when the maximum load was 8 *g* or more the required total time of exposure to loads in excess of 3, 4, or 5 *g* was about the same, regardless of the maximum load applied. Thus the mean time of exposure to loads above 3 *g* producing loss of consciousness was 4·2 seconds (range 3·88 to 4·4 seconds). The period of unconsciousness lasted from 5 to 10 seconds following exposure to accelerations of 8 to 15 *g*, and was not preceded by the classic " black-out ". No electrocardiographic or electroencephalographic abnormalities were observed during the application of high positive acceleration. Immediately after exposure the behaviour of the subjects was normal, apart from minor confusion lasting up to 5 minutes in a few instances. No petechiae were seen in the limbs, and there was no evidence of permanent damage of any kind. The fact that the duration of cerebrovascular stasis caused by exposure to accelerative stress which is necessary to produce loss of consciousness is less than the mean time required to produce unconsciousness by occlusion of the carotid and vertebral arteries may be due to partial drainage of the cerebral capillaries in the former condition, so that less blood (and hence less available oxygen) remains in the brain than is the case after simple occlusion of the cervical blood vessels.

J. A. Armstrong

Anaesthetics

1186. **A New Ultra-short-acting Narcotic.** (Über ein neues Ultrakurznarkotikum)
H. Weese and F. H. Koss. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **79**, 601–604, April 16, 1954. 4 figs., 9 refs.

The new narcotic here described, " baytinal " (5 : 5-allyl-(2′-methylpropyl)-thiobarbiturate sodium), is an ultra-short-acting barbiturate, suitable for use as an anaesthetic for ambulant patients. For adult patients 2 to 3 ml. of a 10% solution is given quickly, followed by 1 to 3 ml. after 1 to 1½ minutes. A further 3 to 4 ml. may be given later if required, but the total dosage should never be more than 1 g.

At the Surgical Clinic of Düsseldorf Medical Academy, 350 patients have been treated with this agent and a variety of surgical procedures of under ten minutes' duration have been performed without mishap, although those treated included many seriously ill and weak patients. The pulse rate and blood pressure remained constant, and neither excitement nor vomiting occurred after administration of the analgesic. Good muscular relaxation was obtained by the addition of succinylcholine. A few minutes after completion of the operation the patients could walk out of the operating theatre and within 30 minutes they were ready to go home. A retrograde amnesia generally occurred for about 10 minutes after the operation. As a euphoric state persisted for one to 2 hours, however, it is advised that patients should not, for example, drive a car for the rest of the day. *Robert Hodgkinson*

1187. **The Control and Management of Hypertensive Crises Developing during Surgical Procedures**
A. M. Riskin, D. Semeraro, and R. W. Robertazzi. *Anesthesiology* [*Anesthesiology*] **15**, 262–272, May, 1954. 6 figs., 11 refs.

It is first pointed out that the concept of controlled hypotension is a relatively new one. Blood pressure can be reduced by ganglionic and effector-organ blocking agents; similarly blood pressure can be raised by drugs which act as peripheral vasoconstrictors or which increase cardiac output. These methods may be used alone or in combination to maintain blood pressure at any previously specified and selected level. Hexamethonium bromide has been used extensively to reduce normal blood pressure to a hypotensive level.

A method of controlling hypertensive crises during anaesthesia is described in this paper from the University Hospital, New York. The need for the control of such crises became evident during cystoscopic examination of paraplegic patients with spinal-cord transection at the 5th thoracic segment or above, and of quadraplegic patients. In these patients distension of a hollow viscus, particularly the bladder or rectum, results in vasoconstriction in the extremities, a rise in blood pressure, a decrease in the pulse rate, and changes of rhythm, with vasodilatation in the neck, face, and nasal mucosa (mass autonomic reflex). (Anaesthesia charts showing these changes are reproduced.) In several cases of spinal-cord transection the hypertension and the accompanying headache were controlled by administration of hexamethonium bromide. This drug was also given to control the hypertension in 2 patients with expanding intracranial lesions, and in one patient operated on for Graves's disease. Altogether the authors have used this method successfully in 24 cases. *W. Stanley Sykes*

1188. **Hypertension during Anesthesia in Patients with Spinal Cord Injuries**
B. J. Ciliberti, J. Goldfein, and E. A. Rovenstine. *Anesthesiology* [*Anesthesiology*] **15**, 273–279, May, 1954. 2 figs., 6 refs.

In cases of spinal-cord injury the part of the cord distal to the lesion not only recovers its reflex function but becomes highly excitable. A " mass reflex " occurs on distension of the bladder or other stimulus, and causes sweating, severe headache, slowing of the pulse, hypertension, convulsions, and even loss of consciousness. During anaesthesia this paroxysmal hypertension may cause difficulty in haemostasis or provoke cerebrovascular accidents. In patients with lesions at the 6th thoracic segment or below there are still areas in the upper extremities and splanchnic region which can provide compensatory vasodilatation, and hypertension does not occur; but in patients with lesions at the 5th thoracic segment or above there is no physiological compensation for this reflex.

The authors, from the Veterans Administration Hospital, Bronx, New York, report 27 cases of lesions at the 5th thoracic segment or above in which general anaesthesia was given on 54 occasions. On 23 occasions (42·5%) there was a rise in systolic pressure of 55 mm. Hg. In one case haemorrhage was so profuse that cessation of the operation was considered, but hexamethonium bromide reduced the hypertension at once. Tetraethylammonium chloride was also effective in blocking the reflex. In 13 instances spinal analgesia prevented the reflex, but preliminary studies showed that bilateral paravertebral blocks were ineffective. *W. Stanley Sykes*

1189. **Effect of Controlled Hypotension on Cerebral Function and Circulation**
J. W. Saunders. *Lancet* [*Lancet*] **1**, 1156–1158, June 5, 1954. 29 refs.

In view of reports of neurological complications thought to be due to cerebral ischaemia following the induction of controlled hypotension, the author has investigated, at Otago University Medical School, Dunedin, the cerebral blood flow and arterio-venous oxygen difference in patients subjected to this procedure.

Samples of cerebral venous blood were taken from the cranial venous sinuses of 8 anaesthetized patients undergoing craniotomy, hypotension being induced with hexamethonium bromide and by pneumatic suction to the legs, the patient being very nearly horizontal (average tilt 5 degrees); samples of arterial blood were taken at the same time. The mean cerebral arterio-venous oxygen difference was found to be 4·8 vols. %, that is, it was 2·3 vols. % below the average figure of 7·1 vols. % reported for healthy conscious people. The estimated cerebral blood flow during the hypotension was approximately equal to that of a normal healthy individual. Since there is a fall in cerebral vascular resistance produced by the hexamethonium bromide and a decreased cerebral oxygen demand during anaesthesia, the author believes that the cerebral blood flow was more than adequate to meet the metabolic demands of the brain.

In a further experiment on 10 conscious healthy individuals in the upright position, their blood pressure was reduced by hexamethonium bromide to 60 mm. Hg without loss of consciousness. The author concludes therefore that when the systolic pressure of patients is reduced to 60 mm. Hg by hexamethonium bromide combined with suction to the legs and the patient is kept almost horizontal—this is emphasized—the cerebral blood flow is not decreased and remains adequate for the metabolic needs of the brain. *A. M. Hutton*

1190. **Vomiting and Regurgitation during Anaesthesia**
E. J. O'MULLANE. *Lancet* [*Lancet*] **1**, 1209–1212, June 12, 1954. 1 fig., 2 refs.

At St. Thomas's Hospital, London, the author has investigated the effects of relaxants and posture on regurgitation and vomiting during general anaesthesia, variations in intragastric pressure and the competence of the cardiac and cricopharyngeal sphincters each being studied separately. The subjects were conscious volunteers and patients undergoing anaesthesia for various operations. In all cases polythene tubing 1 to 2 mm. in diameter was passed into the stomach and 500 to 1,000 ml. of saline introduced. Pressures were measured either directly on a water manometer or by means of a tambour recording on a moving drum.

The factors affecting intragastric pressure were investigated in 22 subjects, in 10 of whom the abdomen was distended and in 12 concave in the supine position. The pressures in these two groups contrasted strongly in the conscious subject and showed but little change during light and deep anaesthesia. When full doses of muscle relaxants were given, the average pressure in the former group was +9 cm. H_2O, and in the latter −3 cm. H_2O, in the supine position. Adoption of the lithotomy position caused a rise in average pressure to +15 cm. H_2O in the former group, but very little fall in pressure resulted from the 20% foot-down tilt. Under the same conditions the intragastric pressure in the group without distension showed no gross variation with posture.

The factors affecting the cardia were investigated in 9 anaesthetized and fully relaxed subjects, in whom a constant intragastric pressure of 15 to 20 cm. H_2O was obtained by placing sandbags on the abdomen. Competence of the cardia was maintained after the administration of full doses of relaxant drugs and ganglion-blocking agents and after local infiltration of the cardia with amethocaine. Incompetence was, however, induced in two ways: (1) in 2 cases under deep anaesthesia with cyclopropane, retaining spontaneous respiration, the mechanism of vomiting was mimicked by increasing the intragastric pressure and at the same time obstructing the airway during inspiration, when saline invariably entered the oesophagus; (2) in 3 cases traction was applied to the very mobile mucous layer proximal to the cardio-oesophageal junction by means of a cuffed tube, when saline again invariably entered the oesophagus.

The competence of the cricopharyngeal sphincter was investigated by introducing 200 ml. of saline into the oesophagus while maintaining an intragastric pressure of more than 10 cm. H_2O during light anaesthesia. There was no leakage into the pharynx even with the patient in the Trendelenburg position, but incompetence occurred in the head-down position during fairly strong manual inflation of the lungs, on deepening the anaesthesia, and after giving small doses of relaxant drugs. Fluid pooled in the pharynx, however, could not be dislodged into the oesophagus by positive pressure inflation or by heavily loading the expiratory valve; only by making the patient gag could fluid be displaced in this direction.

The author concludes from these experiments that the adoption of the foot-down position during induction of anaesthesia with relaxants in the patient whose stomach may not be empty, as advocated by Morton and Wylie (*Anaesthesia*, 1951, **6**, 190), is safe because the cardia retains its competence even under total paralysis. He also concludes that if vomiting is allowed to occur after the induction of anaesthesia but before the onset of paralysis, any gastric contents present in the pharynx will tend to enter the trachea, as the one-way action of the cricopharyngeal sphincter will prevent entry into the oesophagus, so that simultaneous hypnosis and relaxation should therefore be aimed at, and that the dangers of regurgitation will be increased by inspiratory stridor or obstruction of the respiration by "ball-valving" of the tongue, especially when intragastric pressure is high, as in the lithotomy position.

[The author is to be congratulated on planning experiments which answer so satisfactorily hitherto unexplained points of common clinical experience. The reader should refer to the original paper for practical details of the investigations.] *Michael Kerr*

1191. **Coronary Blood Flow and Myocardial Metabolism in Hypothermia**
W. S. EDWARDS, S. TULUY, W. E. REBER, A. SIEGEL, and R. J. BING. *Annals of Surgery* [*Ann. Surg.*] **139**, 275–281, March, 1954. 1 fig., 25 refs.

1192. **Effect of Efocaine on the Oral Mucous Membrane**
J. D. PIRO, E. E. SPROUL, E. V. ZEGARELLI, and A. H. KUTSCHER. *Anesthesiology* [*Anesthesiology*] **15**, 397–406, July, 1954. 4 figs., 10 refs.

See also Cardiovascular System, Abstract 1045.

Radiology

RADIODIAGNOSIS

1193. **Descriptive Classification of Pulmonary Shadows. A Revelation of Unreliability in the Roentgenographic Diagnosis of Tuberculosis**
R. R. NEWELL, W. E. CHAMBERLAIN, and L. RIGLER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 566–584, April, 1954. 10 figs., 6 refs.

During an investigation of the comparative value of radiology and photofluorography in the diagnosis of pulmonary tuberculosis (*J. Amer. med. Ass.*, 1947, **133**, 359) it was noted that radiologists frequently failed to agree in the interpretation of their findings. Following this publication a board was set up under the auspices of the United States Public Health Service with the following objects: (1) to determine the reliability of *x*-ray diagnosis in tuberculosis; (2) to attempt a classification of pulmonary lesions, as seen on radiographs, which would give " optimal reliability "; and (3) to estimate and " prove the validity of such a classification ".

The present authors examined several large series of radiographs but their individual description and assessment of the lesions showed very poor agreement. Moreover, when one of them read a series twice, the second interpretation often did not agree with the first. Various attempts were made to improve these results, but without material success. They state, in their summary of the paper, that " classification of possibly tuberculous pulmonary lesions on the basis of roentgenographic appearance is not very reliable. There is not much to choose among the three approaches to the problem: (*a*) an objective description of the lesion, (*b*) a quasi-pathologic classification, and (*c*) a subjective judgment of activity. All are less reliable than the classification of extent in common use (minimal, moderately advanced, far advanced) ".

The paper contains a detailed description and analysis of the methods employed and the results. Although the authors failed in two of the three objects of the investigation they hope that the report will be of value to those undertaking a similar study in the future.

Sydney J. Hinds

1194. **Cavitation in the Lungs of Child and Infant**
A. M. RACKOW. *British Journal of Radiology* [*Brit. J. Radiol.*] **27**, 330–339, June, 1954. 12 figs., 9 refs.

1195. **The Roentgen Diagnosis of Polycystic Kidneys.** [In English]
L. BILLING. *Acta radiologica* [*Acta radiol. (Stockh.)*] **41**. 305–315, April, 1954. 11 figs., 2 refs.

In an attempt to determine points of differentiation between the early stage of polycystic disease and normal variations in the shape and size of the kidney and renal pelvis, the author, working at Sahlgrenska Hospital, Gothenburg, Sweden, has compared the radiological appearances in 14 confirmed cases of polycystic disease of the kidneys with the urograms of 50 patients whose kidneys were judged clinically and radiologically to be normal.

From this investigation he concludes that the following findings are suggestive of polycystic disease. (1) A lobular outline, though not very frequently seen, is very suggestive. (2) Increased length of the kidney; in practically every case of polycystic disease the length of the kidney, measured in films taken with a focus–film distance of 100 cm., was 14 cm. or over, whereas only one out of the 100 normal kidneys measured 14 cm. (3) Increased thickness of the parenchyma; in the pyelogram, if the distance between the lateral outline and the nearest laterally directed minor calyx is taken as an index of the thickness of the parenchyma, this distance was found in the majority of polycystic kidneys to exceed the upper limit of normal, that is, 3 cm. (4) Elongation of a calyx is difficult to judge, but if pronounced is characteristic. (5) The finding of multiple deformities of calyces, due to pressure by an adjacent cyst, is almost pathognomonic.

Among less significant signs are lateral displacement of the renal pelvis, as judged by the distance from the pelvis to the spinal column being greater than the width of a vertebral body; this sign, however, may be found in the normal kidney. Similarly, a pelvis whose long axis is parallel to the spine, or whose ampulla is horn-shaped and has settled obliquely or horizontally, is a feature of relatively little value, although the horizontal position is rare in the normal kidney.

In aortograms the branches of the renal artery may show stretching, but this sign may occur in all enlarged kidneys. At the nephrographic stage, however, after injection of the aorta, the appearances are pathognomonic, the opaque cortex showing a worm-eaten appearance due to the presence of innumerable cysts. In the author's view aortography should seldom be necessary, but it is a deciding factor in the differential diagnosis of doubtful cases.

Kenneth A. Rowley

1196. **Hirschsprung's Disease. Roentgen Diagnosis in Infants**
R. G. MCDONALD and W. A. EVANS. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **87**, 575–585, May, 1954. 4 figs., 16 refs.

After defining Hirschsprung's disease and reviewing the literature the authors discuss 16 cases seen at the Children's Hospital, Detroit, especially the radiological diagnosis. Since the colon of the normal infant can be distended to a marked degree, the diagnosis of Hirschsprung's disease depends upon detection of abnormal stasis of barium and a persistent disparity in calibre of two segments of the colon. In 6 cases, however, no disparity was detected at the original examination, and the authors

point out that although this may manifest itself later, many infants may die before any pronounced degree of dilatation and hypertrophy of the proximal segment occurs. In the normal infant there is usually a prompt and forceful emptying of the colon following a barium enema; in the present series retention of the barium, often up to 48 hours, was a prominent feature, and the authors therefore suggest that this retention may be an important early sign of Hirschsprung's disease.

Sydney J. Hinds

1197. **The Roentgenologic Appearance of the Small Intestine in Sprue. Long-term Studies with Special Reference to Differential Diagnosis**

D. ADLERSBERG, R. H. MARSHAK, H. COLCHER, S. R. DRACHMAN, A. I. FRIEDMAN, and CHUN-I WANG. *Gastroenterology* [*Gastroenterology*] **26**, 548–581, April, 1954. 10 figs., 47 refs.

The authors have studied the radiological appearances in the small intestine of 40 patients with the sprue syndrome at Mount Sinai Hospital, New York. The observation period ranged from 1 to 17 years. An opaque meal consisting of 8 fl. oz. (227 ml.) of barium (by volume) diluted to 16 oz. (454 ml.) with water was given, the first and second films being taken at 15-minute intervals and subsequent films at intervals of 30 to 60 minutes until the barium had left the small intestine. In some cases an additional 4 to 6 oz. (114 to 170 ml.) of the mixture was necessary. Any abnormal finding was always verified by repeating the examination.

The findings were normal in 3 cases, but in the remainder they exhibited the following characteristics. (1) *Dilatation.* This was most marked in the middle and distal portions of the jejunum, its degree varying with the severity of the disease. The authors state that dilatation in sprue is more marked than in the other conditions which simulate it radiologically. (2) *Segmentation.* A " late " form is described, seen when the small intestine is in process of evacuation or when evacuation has just been completed, in which medium-sized loops are found, from 4 to 10 cm. in length, most commonly in the ileum. The " early " form is seen as soon as the intestine is filled, the segments being small, numerous, and contracted, and occurring throughout the length of the small intestine. (3) *Hypersecretion.* The shadow of the meal has a granular quality, with coarser flocculation through the filled segments. (4) *Moulage sign.* This is seen in the proximal jejunum, where the normal folds become smooth and appear effaced. It is observed in advanced cases with atony and atrophy of the bowel wall. (5) *Scattering.* The faint irregular stippling normally seen as the meal leaves the small bowel is replaced by larger, amorphous mottling best seen in the jejunum or proximal ileum.

The authors studied the effect of treatment, but were unable in every case to correlate clinical improvement with radiological improvement. They discuss in some detail the differential diagnosis of sprue from such conditions as tuberculosis of the small bowel and ileojejunitis, and conclude that the findings described are sufficiently distinctive for differentiation from these other conditions.

L. G. Blair

1198. **Pantomography in Theory and Use.** [In English] Y. V. PAATERO. *Acta radiologica* [*Acta radiol. (Stockh.)*] **41**, 321–335, April, 1954. 12 figs., 9 refs.

Pantomography is a technique whereby tomograms of curved layers of an object may be recorded, that is, the pantomogram may be regarded as a panoramic radiograph of the curved layer. In the technique here described from the Institute of Dentistry, University of Helsinki, the patient's head is placed within a ring mounted on a rotating motor-driven chair whose axis of rotation corresponds to the centre of the ring, and a circular plate is rotated in the horizontal plane by friction of its edge against that of the ring. The *x*-ray film is curved to the shape of the plane of the object to be recorded (for example, the patient's jaw) and placed on edge on this plate. As the plate and ring are of the same diameter, all points an equal distance from the rotational axes have the same linear angular velocity. Thus, if the *x*-ray film forms part of a " cylinder " placed at a certain distance from the vertical axis of rotation, the cylindrical plane of an object at the same distance from the axis of rotation of the object-ring will be in register on the film as the film and object rotate through the stationary *x*-ray beam. Other planes of the object rotate at a different linear velocity, and will thus be blurred out on the radiograph. The shape and location of the film on the plate therefore determine the shape and situation of the object plane recorded.

The author describes the details of the theory and practice of this technique. He emphasizes that it is necessary to allow for divergence of the *x*-ray beam, and that to do this the film must be placed at a greater distance from the rotational axis than the plane of the object to be recorded. The film is protected from secondary radiation by a lead sheet with a vertical slit placed between the object and the film, and by a Lysholm grid with the lines horizontal. He has successfully applied this technique to examination of the skull and jaws, and has also experimented with pantomograms of the thorax with encouraging results.

[While this and similar techniques represent an ingenious application of the principles of tomography, it is debatable whether the additional information obtained, if any, justifies the time and expense involved in using such procedures in addition to routine methods of radiography and screen and tomographic examination.]

Kenneth A. Rowley

1199. **Minimal Pneumotomography of the Brain.** (La pneumostratigraphie encéphalique à minima. Étude anatomo-radiologique)

P. BÉTOULIÈRES, R. PALEIRAC, R. LABAUGE, and J. BASSÈDE. *Journal de radiologie, d'électrologie et Archives d'électricité médicale* [*J. Radiol. Électrol.*] **35**, 27–30, 1954. 8 figs.

The authors present a description of the technique of lumbar pneumo-encephalography combined with tomography which they have now employed in some 20 cases at the Faculty of Medicine, Montpellier. The cardinal point of the method is that only a minimal quantity of air is injected, the total amount given for an examination

of both the basal cisterns and the ventricles not exceeding 30 or 40 ml. They describe in detail the technique by which either the basal cisterns or the ventricles may be filled, the patient's head being maintained in hyperextension and hyperflexion respectively. Their practice is to fill the basal cisterns first. Tomography in the lateral position (three layers, the central one of which is in the midline) is then carried out, and a plain film is taken in addition.

Next, the ventricles are filled, also by the lumbar route, and a further series of lateral tomograms are taken, plain lateral views being obtained at the same time if desired. Finally, the lateral ventricles are examined in more detail by postero-anterior tomography. The authors give mean measurements, obtained from their series of 20 cases, for the position of the aqueduct.

[There are a number of points in the authors' technique which are contrary to accepted practice in Great Britain. For example: (1) It is usual to fill the ventricles before the basal cisterns, since prior filling of the basal cisterns may cause difficulty in introducing air into the ventricles. (2) The amount of 20 ml. of air recommended by the authors for injection into the cisterns is rather more than is usually thought necessary here. (3) The method necessitates having a tomographic apparatus capable of taking pictures in the vertical position—but this is not usually available. (4) Good radiographs in the lateral and postero-anterior positions demonstrate the 4th ventricle and aqueduct quite as clearly and precisely as do the tomograms here reproduced. On the other hand, it is probable that greater detail in visualization of the basal cisterns is obtained by the authors' method of tomography.] *G. H. du Boulay*

1200. **The Role of Mediastinal Pneumotomography in the Study of Congenital Heart Disease.** (L'apport de la pneumostratigraphie médiastinale dans l'étude des cardiopathies congénitales)

G. GIRAUD, P. BÉTOULIÈRES, H. LATOUR, P. PUECH, M. PÉLISSIER, and F. LEVÈRE. *Journal de radiologie, d'électrologie et Archives d'électricité médicale* [*J. Radiol. Électrol.*] **35**, 37–41, 1954. 8 figs.

The authors describe a method for the study of congenital heart disease by means of tomography of the mediastinum into which air has been introduced. [The exact technique of the introduction of air or oxygen is not given in detail.] The authors state that for transdiaphragmatic insufflation of 1,500 to 2,000 ml. of air both the precoccygeal and retropubic routes are equally satisfactory. Tomography is carried out in posterior, lateral, and oblique positions, the degree of obliquity being determined by a preliminary screening of the patient.

They have found that by this means the aorta is seen with clarity, and the origins of the great vessels and the site, relations, size, and length of the narrowed arterial segment in coarctation can be well visualized. The authors are convinced that this method of examination has a great advantage over aortography in that the poststenotic part of the aorta is seen quite clearly, and the larger anastomotic vessels are also demonstrated. The method is also valuable for the detection of a persistent ductus arteriosus and for the demonstration of anomalous pulmonary veins. It is claimed also that by this technique the most exact idea of the relative sizes of the various chambers of the heart may be obtained.

G. H. du Boulay

RADIOTHERAPY

1201. **An Evaluation of the Clinical Use of a Strontium 90 Beta-ray Applicator with a Review of the Underlying Principles**

H. L. FRIEDELL, C. I. THOMAS, and J. S. KROHMER. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **71**, 25–39, Jan., 1954. 8 figs., 10 refs.

In 1950 the authors described a beta-ray eye applicator incorporating radioactive strontium (^{90}Sr) as the source, and in this paper its clinical use at the Western Reserve University Hospitals, Cleveland, Ohio, is evaluated. Radioactive strontium was chosen for treating corneal diseases because of its long half-life (22 years), its energetic beta particles, and the absence of gamma rays (which would penetrate to the lens). Two applicators were used, one with a window thickness of 100 mg. per sq. cm., and the other, which was used in most cases, with a window thickness of 20 mg. per sq. cm. The beta-ray output was 30 r.e.p. per second, and the depth dose was 41% at 1 mm. and 19% at 2 mm. The authors found slit-lamp examination to be invaluable in determining the depth of the corneal lesion and therefore in estimating the amount of radiation necessary. By analogy with general radiation therapy, the dose was fractionated, usually at weekly intervals, this allowing individualization of the radiotherapy according to the response and enabling the total dose to be kept as low as possible. In using the applicator the eye was anaesthetized with 1% " pontocaine " (amethocaine), the lids immobilized, and the applicator placed in full contact with the corneal process; in corneal disease, treatment was given along the limbus to affect vessels near their origin, it being imperative that the centre of the cornea be avoided whenever possible.

Of a total of 137 cases treated, 65 were cases of corneal vascularization, those with superficial and newly formed vessels showing the best response. The average dose in these cases was 6,000 r.e.p., the highest being 12,000 r.e.p., and the authors now recommend a dose of 1,800 r.e.p. per treatment at weekly intervals, stating that most superficial lesions will respond to doses of about 6,000 r.e.p. For vascularization immediately after keratoplasty they recommend a dose of 1,800 r.e.p. within 48 hours of operation and repeated every 2 or 3 days up to a maximum of 9,000 r.e.p., the average total dose being considerably less. The deep vascularization of interstitial keratitis generally required larger doses than the superficial type. In cases of pterygium the best results were obtained by surgical removal and postoperative irradiation; only thin, newly formed pterygia should be considered for beta-irradiation

initially. Satisfactory results were also noted in the treatment of vernal catarrh, early cases responding best and the limbal type needing less radiation than the palpebral. Conjunctival tumours treated with satisfactory results included papilloma, haemangioma, and chalazion. Tuberculous sclerokeratitis and chronic conjunctivitis also responded well to beta irradiation. [Reference should be made to the original paper for details of the dosages employed for the above conditions and for a small miscellaneous group of other disorders.]

The authors observed no complications of any consequence in using this applicator. Although no lenticular opacities have appeared during the 4 years of its use, it is still possible that they may appear later. However, the authors observed no cataracts resulting from the use of a radon applicator, which gave a much larger dose to the lens, over a period of more than 10 years.

Arthur Jones

1202. **Problems of Dosimetry in the Use of Radioactive Iodine in the Treatment of Cancer of the Thyroid Gland.** (Problèmes de dosimétrie posés par l'utilisation de l'iode radioactif dans le traitement du cancer de la thyroïde)
R. COLIEZ, M. TUBIANA, and J. DUTREIX. *Journal de radiologie, d'électrologie et Archives d'électricité médicale* [*J. Radiol. Électrol.*] **35**, 22–27, 1954. 8 figs., 11 refs.

1203. **Technique of Treatment of Chordoma of a Lumbar Vertebra with 2 Million Volt *X*-rays Using the Rotation Technique**
M. FRIEDMAN. *Bulletin of the Hospital for Joint Diseases* [*Bull. Hosp. Jt Dis. (N.Y.)*] **14**, 180–187, Oct., 1953 [received May, 1954]. 11 figs., 2 refs.

The author describes a case of chordoma which was successfully treated with *x* rays at 2 million volts. During investigation for severe back pain of 3 months' duration, a man of 44 was found to have an osteolytic tumour involving the right half of the body of the fourth lumbar vertebra. Histological examination of biopsy material showed this to be a chordoma. It was estimated that the posterior edge of the tumour, which was itself about 4 cm. in diameter, was only 1 cm. from the spinal canal.

Past experience has shown these tumours to be extremely radio-resistant, but it was considered that destruction might be possible if a dose of about 7,000 r could be delivered in 5 to 7 weeks. Rotation technique was employed, as it appeared the only reasonable method of delivering the required dose without excessive side-reactions. The contour of the patient was ascertained by means of a body contour meter, the outline transferred to paper, and the position of the tumour indicated. Beam angulation vectors were derived to position the tumour at the centre of rotation and to measure the dosage.

Rotation was carried out, with the patient standing and the tumour centred at the rotational axis, at a rate of one revolution per minute, each treatment lasting 5 to 7 minutes. A tumour dose of 7,200 r was delivered in 47 days to a cylindrical volume 6 cm. in diameter and 6 cm. in height, with no untoward effects on neighbouring structures. At the end of treatment the patient was free from pain, and *x*-ray examination showed that sclerosis of the bone had occurred, with restoration of the normal vertebral contours. *A. M. Jelliffe*

1204. **Radiation Therapy of Pancreatitis**
C. H. HEACOCK and D. J. CARA. *Radiology* [*Radiology*] **62**, 654–659, May, 1954. 17 refs.

The treatment of 53 cases of pancreatitis by *x* irradiation is discussed. Deep *x*-ray therapy is advocated in conjunction with supportive measures in all cases, the prime object being the reduction of pancreatic secretion, though a specific effect upon the inflammatory process is suggested. Treatment was given with 200-kV *x* rays of 2 mm. Cu. H.V.L. through a 15×15-cm. applicator, with a target skin distance of 50 cm. A total dose of 600 r, measured in air, was given at three consecutive daily treatments each of 200 r. Four courses of treatment were necessary for one patient, three for 4 patients, and two for 7 [but the authors do not state the intervals between treatments]. An analysis showed that of the 53 patients (24 males and 29 females aged 23 to 73 years), 10 had undergone cholecystectomy, 5 gastric surgery, and 13 exploratory laparotomy. The condition was diagnosed either by clinical and biochemical examination or at laparotomy. Reference is made to the serum amylase values in 29 cases.

The results of *x*-ray therapy were good in 62%, fair in 29%, and poor in 9%. The authors believe that the early use of *x*-ray therapy prevents abscess formation, necrosis, fibrosis, and, possibly, recurrence. *G. E. Flatman*

1205. **Supervoltage *X*-ray Treatment of Carcinoma of the Bladder**
H. F. HARE, J. G. TRUMP, R. C. GRANKE, and J. ANSON. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **2**, 251–255, April, 1954. 3 figs.

This is an interim communication on the treatment of infiltrating carcinoma of the bladder by rotation therapy with *x* rays at 2 million volts at the Massachusetts Institute of Technology. No attempt is made to give complete technical details, and the results are not given in full. It is stated, however, that good palliation has been obtained, with complete regression of the tumour, at least temporarily, in many cases. Before treatment the patient is placed in the Trendelenburg position and the abdomen firmly bandaged to try to exclude small bowel as far as possible from the pelvis during treatment. The treatment is given with the patient standing on a rotating platform, the tube being directed horizontally at the level of the tumour. The patient rotates about once a minute. A 14-cm. circular field is used, with absorbers placed laterally so as to reduce the size of the field in relation to diameter of the patient's pelvis. A dose of 6,000 to 8,000 r is delivered to the bladder region in 35 treatment days. A tumour dose of 6,000 r was at first thought to be adequate, but frequent local recurrence made it clear that a higher dose is desirable. Severe complications of treatment were not observed, though there was some bladder irritation. *E. Stanley Lee*